TEC Partnership
Grimsby Institute of Further & Higher Education (GIFHE)
Nuns Corner
Grimsby
North East Lincolnshire
DN34 5BQ

Attn: [redacted]
By email to: [redacted]

Date: 12/07/2022
Our ref: FS430957

Dear [redacted],

Supply of Critical review of AMR risks arising as a consequence of using biocides and certain heavy metals in food animal production

Following your tender/ proposal for the supply of Critical review of AMR risks arising as a consequence of using biocides and certain heavy metals in food animal production to Food Standards Agency, we are pleased confirm our intention to award this contract to you.

The attached contract details ("**Order Form**"), contract conditions and the ***Annexes*** set out the terms of the contract between Food Standards Agency for the provision of the deliverables set out in the Order Form.

We thank you for your co-operation to date and look forward to forging a successful working relationship resulting in a smooth and successful delivery of the deliverables. Please confirm your acceptance of the Conditions by signing and returning the Order Form. No other form of acknowledgement will be accepted. Please remember to include the reference number above in any future communications relating to this contract.

We will then arrange for Order Form to be countersigned which will create a binding contract between us.

Yours faithfully,

[redacted]

Commercial Category Manager

Order Form

1. Contract Reference	**FS430957**	
2. Date	14/07/2022	
3. Buyer	**Food Standards Agency** **Clive House** **70 Petty France** **London** **SW1H 9EX**	
4. Supplier	TEC Partnership (Grimsby Institute of Further & Higher Education, GIFHE) Nuns Corner Campus Grimsby DN34 5BQ	
5. The Contract	The Supplier shall supply the deliverables described below on the terms set out in this Order Form and the attached contract conditions ("**Conditions**") and any ***Annexes***. Unless the context otherwise requires, capitalised expressions used in this Order Form have the same meanings as in Conditions. In the event of any conflict between this Order Form and the Conditions, this Order Form shall prevail. Please do not attach any Supplier terms and conditions to this Order Form as they will not be accepted by the Buyer and may delay conclusion of the Contract.	
6. Deliverables	**Goods**	None

	Services	To be performed at **Suppliers premises.** **See Annex 3 – Technical Proposal**
7. Specification	The specification of the Deliverables is as set out in **Annex 2**.	
8. Term	The Term shall commence on **12/07/2022** and the Expiry Date shall be **28/02/2023** unless it is otherwise extended or terminated in accordance with the terms and conditions of the Contract. The Buyer may extend the Contract for a period of up to 3 months by giving not less than 10 Working Days' notice in writing to the Supplier prior to the Expiry Date. The terms and conditions of the Contract shall apply throughout any such extended period.	
9. Charges	The Charges for the Deliverables shall be as set out in **Annex 4 – Charges**.	
10. Payment	All invoices must be sent, quoting a valid purchase order number (PO Number), to: [redacted] Within **10** Working Days of receipt of your countersigned copy of this letter, we will send you a unique PO Number. You must be in receipt of a valid PO Number before submitting an invoice. To avoid delay in payment it is important that the invoice is compliant and that it includes a valid PO Number, PO Number item number (if applicable) and the details (name and telephone number) of your Buyer contact (i.e. Contract Manager). Non-compliant invoices will be sent back to you, which may lead to a delay in payment.	

11. Buyer Authorised Representative(s)	For general liaison your contact will continue to be [redacted] or, in their absence, [redacted]
12. Address for notices	**Buyer:** FSA Commercial Food Standards Agency Foss House Peasholme Green York YO1 7PR [redacted] **Supplier:** TEC Partnership Grimsby Institute of Further & Higher Education (GIFHE) Nuns Corner Grimsby North East Lincolnshire DN34 5BQ
13. Key Personnel	[redacted]

14. Procedures and Policies	The Buyer may require the Supplier to ensure that any person employed in the delivery of the Deliverables has undertaken a Disclosure and Barring Service check. The Supplier shall ensure that no person who discloses that he/she has a conviction that is relevant to the nature of the Contract, relevant to the work of the Buyer, or is of a type otherwise advised by the Buyer (each such conviction a "**Relevant Conviction**"), or is found by the Supplier to have a Relevant Conviction (whether as a result of a police check, a Disclosure and Barring Service check or otherwise) is employed or engaged in the provision of any part of the Deliverables.

Signed for and on behalf of the **Supplier**	Signed for and on behalf of the **Buyer**
[redacted]	

Annex 1 – Authorised Processing Template

Contract:	**FS430957**
Date:	
Description Of Authorised Processing	**Details**
Subject matter of the processing	No personal data is approved to be processed as part of this Contract.
Duration of the processing	
Nature and purposes of the processing	
Type of Personal Data	
Categories of Data Subject	

Annex 2 - Specification

A. THE SPECIFICATION

Background

Antimicrobial resistance (AMR) is the ability of a microorganism to withstand the killing effect of antimicrobials and its emergence limits the therapeutic options available to veterinarians and clinicians. Unless action is taken now to tackle AMR, it has been estimated that there could be 10 million AMR-related deaths worldwide annually by 2050 and cost up to US $100 trillion in cumulative lost economic output[2].

Addressing the public health threat posed by AMR is a national strategic priority for the UK and led to the Government publishing both a 20-year vision of AMR and a 5-year (2019 to 2024) AMR National Action Plan (NAP) which sets out actions to slow the development and spread of AMR. The NAP has adopted an integrated 'One-Health' approach which spans people, animals, agriculture and the environment and calls for activities to "identify and assess the sources, pathways, and exposure risks" of AMR. The FSA are contributing to delivery of the NAP through furthering our understanding of the role of the food chain and AMR, conserving the effectiveness of current treatments through the adoption of good hygiene practices and encouraging the food industry to reduce usage of antimicrobials where possible. AMR genes that result in resistance to critically important antimicrobials are of particular concern to the FSA.

Biocides are products with an active substance that is intended to destroy, deter, render harmless, prevent the action of, or otherwise exert a controlling effect on harmful or undesired organisms[3]. Biocidal products have been used in one form or another for centuries and the more recent development of versatile biocides with limited toxicity for animal tissues such as quaternary ammonium compounds (QACs) has led to increased usage to assist improved hygiene. Biocides are used for a number of reasons in animal production including, the cleaning and disinfecting of buildings as well as decontaminating ponds and equipment in fish farming. They create a barrier against bacteria and viruses by methods such as foot dips outside animal housing. They prevent infection through direct application to animal skin, for example to clean udders of animals used for milk production and preserving specific products such as eggs or semen[4].

Heavy metals are naturally occurring elements that have a high atomic weight and a density at least five times greater than water. Their application in multiple industries such as agriculture has led to their widespread distribution in the environment[5]. The deliberate use of heavy metals in the animal production environment includes application to livestock foot dips to treat skin problems such as

dermatitis[6], however the primary function of heavy metals such as copper and zinc in animal production are nutritional additives in animal feed[7]. Their inclusion maintains various biochemical and physiological functions in animals to preserve health and growth and also to control enteric disease, particularly in the pig and poultry sectors[8]. Heavy metals are often used in higher concentrations than needed to ensure adequate nutrition, therefore an excess may be excreted[6]. This review does not include heavy metal contaminants such as lead and cadmium.

Some biocides and heavy metals used in animal husbandry are able to persist and concentrate in the environment, remaining stable for prolonged periods. It is a concern that bacteria can exhibit resistance to these chemical and metal elements and that the genes encoding for these phenotypes can be located on plasmids that may also contain one or more AMR encoding genes, co-selecting for AMR. These biocidal substances, along with AMR bacteria may be introduced into soil and water through sewage systems, direct excretion, land application of biosolids or animal manures as fertilisers, and irrigation with wastewater or treated effluents[10]. The potential transmission of biocide and heavy metal derived AMR bacteria and resistance genes to humans is a concern. There is some evidence that there is a trend in animal derived AMR isolates caused by biocides that have also been observed in human clinical isolates[11].

This proposed review will help increase our understanding of whether, and to what extent the use of biocides and heavy metals in animal production leads to the development and spread of AMR within the food chain. Also, whether this could potentially lead to greater consumer exposure to AMR bacteria from our food, either directly through consumption of foods derived from animals that have undergone treatment (e.g. the use of heavy metals in animal feed) or indirectly (e.g. exposure of crops to contaminated soil or ground water).

The Specification

Tenders are invited to carry out a:

Critical review of AMR risks arising as a consequence of using biocides and certain heavy metals in food animal production.

We would like to commission a critical review of the scientific literature to enhance our knowledge of the AMR hazards and risks arising as a consequence of biocide and heavy metal use in food animal production. Particularly, it is important to understand the extent to which biocides and heavy metals give rise to the selection and spread of AMR bacteria into the food chain. This information will help to improve our understanding of how current animal husbandry practices impact on AMR, whether further research such as surveillance of biocide and heavy metal usage and associated resistance traits

should be considered and whether steps are needed to reduce the impact of these compounds on AMR.

Details

Proposals submitted **must** include the following key elements:

- A critical review should gather and assess existing data in the literature (including peer-review journals, grey literature, and other sources) to address the following questions/points:
    - Is there evidence to show that biocides and heavy metals used in food animal production have an impact on the development of AMR?
    - How long are biocides and heavy metals able to persist in animal production environments and how does this impact on the development of AMR and associated risks?
    - What evidence is there that biocide and heavy metal associated AMR enters the food chain through products of animal origin or as a result of crop contamination?
    - Is there a potential risk to the consumer from AMR acquired through the use of biocides and heavy metals in food animal production?

We anticipate this project starting in August 2022 with the final report being submitted to the FSA in early-mid January 2023.

- The review should collate and consider literature up to at least the contract start date. However, you should be flexible to possibly extend the search end date to ensure that the review is as 'up to date' as possible particularly if the publication of the final report is delayed. Applicants are advised to carry out a quick search of the literature to estimate the number of papers and include this within their proposals. You should also describe how the grey literature and other information will be identified and sourced for the purpose of this review.
- A clear and structured strategy to the critical review process is expected considering the scope, search methods, the search terms, databases to be searched, screening, inclusion-exclusion criteria including key milestone and deliverable dates and methods used to ensure non-biased searching.
- A key component of this work requires expertise in terms of interpreting the findings of the review. However, the findings will also need to be put into context, in terms of whether the

findings indicate that there is evidence relating to the risks of AMR arising as a result of biocide and heavy metal use in food animal production. Therefore, the applicant(s), either individually or collectively in the research group, should have demonstrable expertise in:

  - Designing and carrying out critical reviews of relevant scientific literature.
  - A molecular microbiological background with sound knowledge of AMR, bacteriology, PCR based techniques
  - Knowledge relating to bacterial gene transfer mechanisms within complex environments such as animal production and the surrounding environment would be highly desirable

- Given the current situation with COVID-19, the applicants should consider the possible risks to the delivery of the study and propose actions to mitigate the foreseen risks as part of the risk register within their proposal.

Outcomes

It is anticipated that the following will be delivered to the FSA as part of this work:

- A full technical report addressing the relevant areas of the study which is suitable for publication on the FSA website. The report should include a lay summary, an executive summary, introduction (including the background and aims/objectives of the review), methodology, findings, discussions, conclusions, list of evidence gaps, recommendations for further work, references and an appendices section. The final report will need to be structured and formatted in accordance with guidelines from the FSA Web Content Accessibility Guidelines. Please note that the final report should be submitted to the FSA **by January 2023** and will undergo an external peer-review process before it can be accepted by the FSA. A draft report should be submitted at least 4 weeks before the final report is due to allow FSA officials sufficient time to comment.
- The critical review should be both transparent and reproducible. A full database of all the relevant publications included in the critical review should be provided to the FSA. The database should be in a format suitable for publication on the FSA website e.g. in an accessible format (for example CSV or Excel).
- Publication of findings from this study in the peer reviewed open access journals and presentations at scientific conferences are encouraged by the FSA. Such material will need to be approved by the FSA prior to being submitted to the journal or presented. It is important that the researcher(s) notify the FSA of the publication date for any papers arising from this study at

the earliest opportunity especially if the findings are contentious and therefore likely to generate media interest.

- The findings of this work are likely to be presented at a future FSA AMR 'show and tell' event, Advisory Committee on the Microbiological Safety of Food (or AMR sub-group) meetings and at a stakeholder meeting if needed.
- Contractors will be expected to assist the FSA in producing documents involved in the publication of the study findings which will include a Q&A document and providing comments on any news story.

Collaborative applications with an appropriate management framework are encouraged to promote well-balanced, innovative proposals that offer value for money and make use of the best available research and analytical approaches.

References:

1. Thomas JC, Oladeinde A, Kieran TJ, Finger JW, Bayona-Vásquez NJ, Cartee JC, et al. Co-occurrence of antibiotic, biocide, and heavy metal resistance genes in bacteria from metal and radionuclide contaminated soils at the Savannah River Site. Microb Biotechnol. 2020 May 3;13(4):1179–200.

2. AMR-Review-Paper-Tackling-a-crisis-for-the-health-and-wealth-of-nations_1-2.pdf [Internet]. [cited 2021 Aug 26]. Available from: https://www.jpiamr.eu/wp-content/uploads/2014/12/AMR-Review-Paper-Tackling-a-crisis-for-the-health-and-wealth-of-nations_1-2.pdf

3. Ministerie van Landbouw N en V. What is a biocidal product? - Board for the Authorisation of Plant Protection Products and Biocides [Internet]. Ministerie van Landbouw, Natuur en Voedselkwaliteit; 2017 [cited 2021 Sep 17]. Available from: https://english.ctgb.nl/biocidal-products/frequently-asked-questions/pre-application-support/biocidal-products/question-and-answer/what-is-a-biocidal-product

4. Biocides: 2. What are the main uses of biocides? [Internet]. [cited 2021 Aug 26]. Available from: https://ec.europa.eu/health/scientific_committees/opinions_layman/en/biocides-antibiotic-resistance/l-2/2-main-uses-biocides.htm

5. Tchounwou PB, Yedjou CG, Patlolla AK, Sutton DJ. Heavy Metals Toxicity and the Environment. EXS. 2012;101:133–64.

6. Yu Z, Gunn L, Wall P, Fanning S. Antimicrobial resistance and its association with tolerance to heavy metals in agriculture production. Food Microbiology. 2017 Jun 1;64:23–32.

7. Hejna M, Gottardo D, Baldi A, Dell'Orto V, Cheli F, Zaninelli M, et al. Review: Nutritional ecology of heavy metals. Animal. 2018 Jan 1;12(10):2156–70.

8. Wales AD, Davies RH. Co-Selection of Resistance to Antibiotics, Biocides and Heavy Metals, and Its Relevance to Foodborne Pathogens. Antibiotics. 2015 Dec;4(4):567–604.

9. EVAL-FARMS: Evaluating the Threat of Antimicrobial Resistance in Agricultural Manures and Slurries - Dimensions [Internet]. [cited 2021 Sep 17]. Available from: https://app.dimensions.ai/details/grant/grant.5125477

10. Yazdankhah S, Skjerve E, Wasteson Y. Antimicrobial resistance due to the content of potentially toxic metals in soil and fertilizing products. Microb Ecol Health Dis. 2018 Dec 11;29(1):1548248.

11. Preharvest and Postharvest Food Safety: Contemporary Issues and Future Directions | Wiley [Internet]. Wiley.com. [cited 2021 Sep 3]. Available from: https://www.wiley.com/en-us/Preharvest+and+Postharvest+Food+Safety%3A+Contemporary+Issues+and+Future+Directions-p-9780470752579

Openness

FSA has values and specific policy on being open and transparent, which includes publishing the full dataset of its research and surveillance studies. Both the lead contractor and their sub-contractors must agree to this openness policy. Any potential issues with this should be highlighted within the proposals.

Cost

The FSA estimates that the cost for this study to be between £30-40k. The onus is on the applicant(s) to provide the costings they believe are reasonable to meet the evidence gap as outlined in this research specification and provide the justification of this within their research proposal. The applicant(s) should be aware that one of the key criteria that all research proposals are evaluated against is 'value for money' which is delivering the research asked for in the research requirement (including the anticipated outputs and benefits) at a competitive price.

Risk

The contractors are to complete a risk register as part of their proposal. They should list any anticipated risk to the delivery of the survey, ranking the likelihood and impact of the risk occurring and offer suggested actions to mitigate these risks.

Data protection

The contractor should outline within their tender whether they anticipate any Personal Data will be collected as part of the surveillance. If so, you should outline in your tender how you will comply with the General Data Protection Regulation (GDPR), recognising the commissioning authority's (the FSA's) role as the 'data controller' and the contractor's role as the 'data processor', and responding to the sections below. If successful and Personal Data is being collected, you may also be asked to carry out a Privacy Impact Assessment (PIA), and a privacy notice may be required, which will be reviewed by the FSA data security team.

Data security

Please confirm in your tender that you have in place, or that you will have in place by contract award, the human and technical resources to perform the contract to ensure compliance with the General Data Protection Regulation (GDPR) and to ensure the protection of the rights of data subjects.

Please provide details of the technical facilities and measures (including systems and processes) you have in place, or will have in place by contract award, to ensure compliance with the GDPR and to ensure the protection of the rights of data subjects. Your response should include, but should not be limited to facilities and measures:

- to ensure ongoing confidentiality, integrity, availability and resilience of processing systems and services
- to comply with the rights of data subjects in respect of receiving privacy information, and access, rectification, deletion and portability of personal data
- to ensure that any consent-based processing meets standards of active, informed consent, and that such consents are recorded and auditable
- to ensure legal safeguards are in place to legitimise transfers of personal data outside the EU (if such transfers will take place)
- to maintain records of personal data processing activities; and
- to regularly test, assess and evaluate the effectiveness of the above measures.

Dissemination

Please outline within your proposal the intentions for publication in the peer reviewed open access journals including any costs associated with this.

Quality

The Applicant(s) for this project should demonstrate that they have an appropriate level of expertise in the specialist areas relevant to biocide and heavy metal use in food animal production and AMR.

Annex 3 – Technical Proposal

Tender Application form for a project with the Food Standards Agency

- Applicants should complete each part of this application as fully and as clearly as possible
- Brief instructions are given in the grey boxes at the start of each section.
- Please submit the application through the Agency's eSourcing Portal (Bravo) by the deadline set in the invitation to tender document.

Lead Applicant's details							
Surname	[redacted]	First Name	[redacted]	Initial		Title	Mr
Organisation	TEC Partnership (Grimsby Institute of Further & Higher Education, GIFHE)	Department	Food Refrigeration & Process Engineering Research Centre (FRPERC)				
Street Address	Nuns Corner Campus						
Town/City	Grimsby	Country	UK	Postcode	DN34 5BQ		
Telephone No	[redacted]	E-mail Address	[redacted]				

Is your organisation is a **small and medium enterprise**. (EU recommendation 2003/361/EC refers http://www.hmrc.gov.uk/manuals/cirdmanual/cird92800.htm)	Yes		No	X

TENDER SUMMARY

TENDER Title

Critical review of AMR risks arising as a consequence of using biocides and certain heavy metals in food animal production

TENDER reference	**FS430957**		
Proposed Start date	18/07/2022	**Proposed**	28/02/2023

1: TENDER Summary AND OBJECTIVES

A. TENDER SUMMARY

Please give a brief summary of the proposed work in no more than 400 words.

The overall aim of this project is to carry out a critical review of the scientific literature on the AMR hazards and risks arising as a consequence of biocide and/or heavy metal use in food animal production and any potential risk to the consumer from AMR acquired through the use of biocides and/or heavy metals in food animal production. It will focus specifically (but not exclusively) on evidence that aids understanding on the extent to which biocides and/or heavy metals give rise to the selection and spread of AMR bacteria and also genes into the food chain. This information will improve the Agency's understanding of how current animal husbandry practices involving such agents impact on AMR, whether further research such as surveillance of biocide and/or heavy metal usage and associated resistance traits should be considered. It will

consider whether steps are needed to reduce the impact of these compounds on the selection and transmission of AMR (bacteria and genes) in the food chain.

It is proposed that the review question will be: "Do biocides and/or heavy metals used in food animal production have an impact on the development of AMR in the food chain?"

The project technical report will critically review the available scientific literature on the AMR hazards and risks arising as a consequence of biocide and/or heavy metal use in food animal production. It will identify, highlight, and recommend where future research and surveillance activities are needed to plug important evidence gaps. A database of the publications included in the review will also be provided. The proposed review will take 8 months to complete.

The project team have recent experience of carrying out such critical reviews on AMR for the Agency and are well positioned to carry out this review for the Agency.

B. OBJECTIVES AND RELEVANCE OF THE PROPOSED WORK TO THE FSA TENDER REQUIREMENT

Objectives

Please detail how your proposed work can assist the agency in meeting it stated objectives and policy needs. Please number the objectives and add a short description. Please add more lines as necessary.

Objective Number	Objective Description
01	**LITERATURE SEARCH:** To carry out a structured literature search of appropriate bibliographic databases and sources to compile a broad data set of as many potentially relevant articles pertaining to the impact of biocides and/or heavy metals used in food animal production on the development of AMR in food as possible. A record of all identified articles will be complied and recorded.
02	**Article screening:** To screen the compiled data set of potentially relevant articles and select relevant articles for data extraction. To ensure transparency a record will be kept of all articles determined as not relevant and reasons for their exclusion.
03	**Data extraction and analysis:** To extract, and analyse, pertinent data from articles that have been selected as containing important information on the development of AMR by the use of biocides and/or heavy metals used in food animal production.
04	**Data synthesis and review completion:** To synthesise the extracted data from articles into a formal review report in order to establish what existing data and understanding there is on the impact of biocides and/or heavy metals used in food animal production on the development of AMR. The review will identify what is known and what data gaps remain and provide recommendations for further work.
05	**Dissemination:** To disseminate the findings of the project (by formal report, peer-reviewed publication, and presentations) to key stakeholders to inform them of the impact of biocides and/or heavy metals used in food animal production on the development of AMR and where further work is required.

2: DESCRIPTION OF APPROACH/SCOPE OF WORK

A. Approach/SCOPE OF WORK

Please describe how you will meet our specification and summarise how you will deliver your solution. You must explain the approach for the proposed work. Describe and justify the approach, methodology and study design, where applicable, that will be used to address the specific requirements and realise the objectives outlined above. Where relevant (e.g. for an analytical survey), please also provide details of the sampling plan.

Project aim and scope

The overall aim of this project is to carry out a broad critical review of the available scientific literature to assess the impact of biocides and/or heavy metals used in food animal production on the development of AMR and any potential risk to the

consumer from AMR acquired through the use of biocides and/or heavy metals in food animal production.

It is proposed that the review question will be: “Do biocides and/or heavy metals used in food animal production have an impact on the development of AMR in the food chain?”

The review will address the following questions/points (terms of reference):

- Is there evidence in the literature to show that biocides and/or heavy metals used in food animal production have an impact on the development of AMR?
- How long are biocides and/or heavy metals (used in food animal production) able to persist in animal production environments and how does this impact on the development of AMR and associated risks?
- What evidence from the literature is there that biocide and/or heavy metal associated AMR enters the food chain through products of animal origin or as a result of crop contamination?
- Is there a potential risk to the consumer from AMR acquired through the use of biocides and/or heavy metals in food animal production?

A central question is whether the release of chemicals like biocides (in particular disinfectants) and/or heavy metals from food animal production has the potential to create local concentrations where AMR can emerge and spread (as bacteria or genes) and whether this presents a potential risk to the consumer as a result. This of course will depend on the organism with resistance and/or the ability for the resistance to be transferable.

Background and rationale

For the interpretation of AMR in this study, the WHO definition will be applied (WHO, 2018): “Antimicrobial resistance is resistance of a microorganism to an antimicrobial drug that was originally effective for treatment of infections caused by it. It is known that resistant microorganisms (including bacteria, fungi, viruses and parasites) are able to withstand attack by antimicrobial drugs, such as antibacterial drugs (e.g., antibiotics), antifungals, antivirals, and antimalarials, so that standard treatments become ineffective and infections persist, increasing the risk of spread to others”.

Antimicrobial resistance (AMR) is a complex issue driven by a variety of interconnected factors enabling microorganisms to withstand the killing or microstatic effects of antimicrobial agents, such as antibiotics, antifungals, disinfectants, preservatives. Microorganisms may be inherently resistant to such agents or can change and adapt to overcome the effects of such agents. Microorganisms can acquire antimicrobial resistance genes (ARGs) through mutation or by acquiring foreign DNA that encodes AMR genes (ARGs). The widespread use of antimicrobial agents is known to result in selection for AMR in microorganisms. AMR and ARGs are a major public health issue worldwide and it is estimated that unless action is taken now to tackle AMR the global impact of AMR could be 10 million deaths annually by 2050 and cost up to US $100 trillion in cumulative lost economic output (O’Neill Report, 2014).

Addressing the public health threat posed by AMR is a national strategic priority for the UK and led to the Government publishing both a 20-year vision of AMR and a 5-year (2019 to 2024) AMR National Action Plan (NAP) which sets out actions to slow the development and spread of AMR with a focus on antimicrobials. The NAP used an integrated ‘One-Health’ approach which spanned people, animals, agriculture, and the environment and calls for activities to “identify and assess the sources, pathways, and exposure risks” of AMR. The FSA have and are continuing to contribute to delivery of the NAP through furthering our understanding of the role of the food chain and AMR, conserving the effectiveness of current treatments through the adoption of good hygiene practices, and encouraging the food industry to reduce usage of antimicrobials where possible. ARGs that result in resistance to critically important antimicrobials are of particular concern to the FSA.

It is recognised that anthropogenic, commensal, and environmental bacteria all contribute to the reservoir of ARGs collectively forming the antimicrobial resistome (Wright, 2007). AMR may be intrinsic or acquired by transfer mechanisms (Verraes *et al.*, 2013). AMR may be transferred from one generation to the next by vertical gene transfer, acquired because of mutation (e.g., genomic point mutations) [which in turn is passed on vertically], or the acquisition of ARGs within the same species or between different bacterial species by horizontal gene transfer [HGT] (Verraes *et al.*, 2013; Munita & Arias, 2016). Bacteria may be resistant to just one antimicrobial agent or to many classes of agent (multi-resistant or multi-drug resistant; MDR), with cross-resistance depending on which ARGs and other mechanisms of resistance are present (such as, enzymatic, permeability barriers, and efflux pumps), as will be discussed in detail further below. This can make infections caused by these organisms difficult to treat and cause illness to persist, with recognised extra costs and increased morbidity and mortality (Likotrafiti *et al.*, 2018).

As previously mentioned, ARGs in AMR bacteria can be transferred to other bacteria through Horizontal Gene Transfer (HGT). Thus, commensal non-pathogenic AMR bacteria can act a reservoir for ARGs and transfer resistance to non-resistant human pathogenic bacteria (Bengtsson-Palme, 2017). HGT is driven by mobile genetic elements (MGEs), such

as plasmids, integrons, and transposons, that facilitate the movement, transfer, and integration of genes between cells (Bennett, 2008). ARGs are not always associated with cultivable 'live' bacteria (Figure 1). Viable but non-culturable bacteria (VBNC) may express genes after "lethal" treatments (James et al., 2021). Non-cellular ARGs, which also cover genes encapsulated in membrane vesicles (MVs), bacteriophages, or gene transfer agents (GTAs), can persist after disinfection, and can transfer to recipient bacteria in the absence of a live donor bacteria (Woegerbauer *et al.*, 2020; James *et al.*, 2021). The frequency of HGT largely depends on the properties of the MGEs, MVs, or bacteriophages, the characteristics of the donor and recipient populations, and the environment (Verraes *et al.*, 2013; Rossi *et al.*, 2014). There are three main canonical mechanisms of HGT through which this can occur: (1) conjugation, (2) transformation, or (3) transduction. Though, as noted by Verraes *et al.* (2013), Hall *et al.* (2017), and ourselves (James *et al.*, 2021), among others, other less well recognized mechanisms of DNA transfer may occur. These processes are described in detail in reviews such as that by Verraes *et al.* (2013) and James *et al.* (2021).

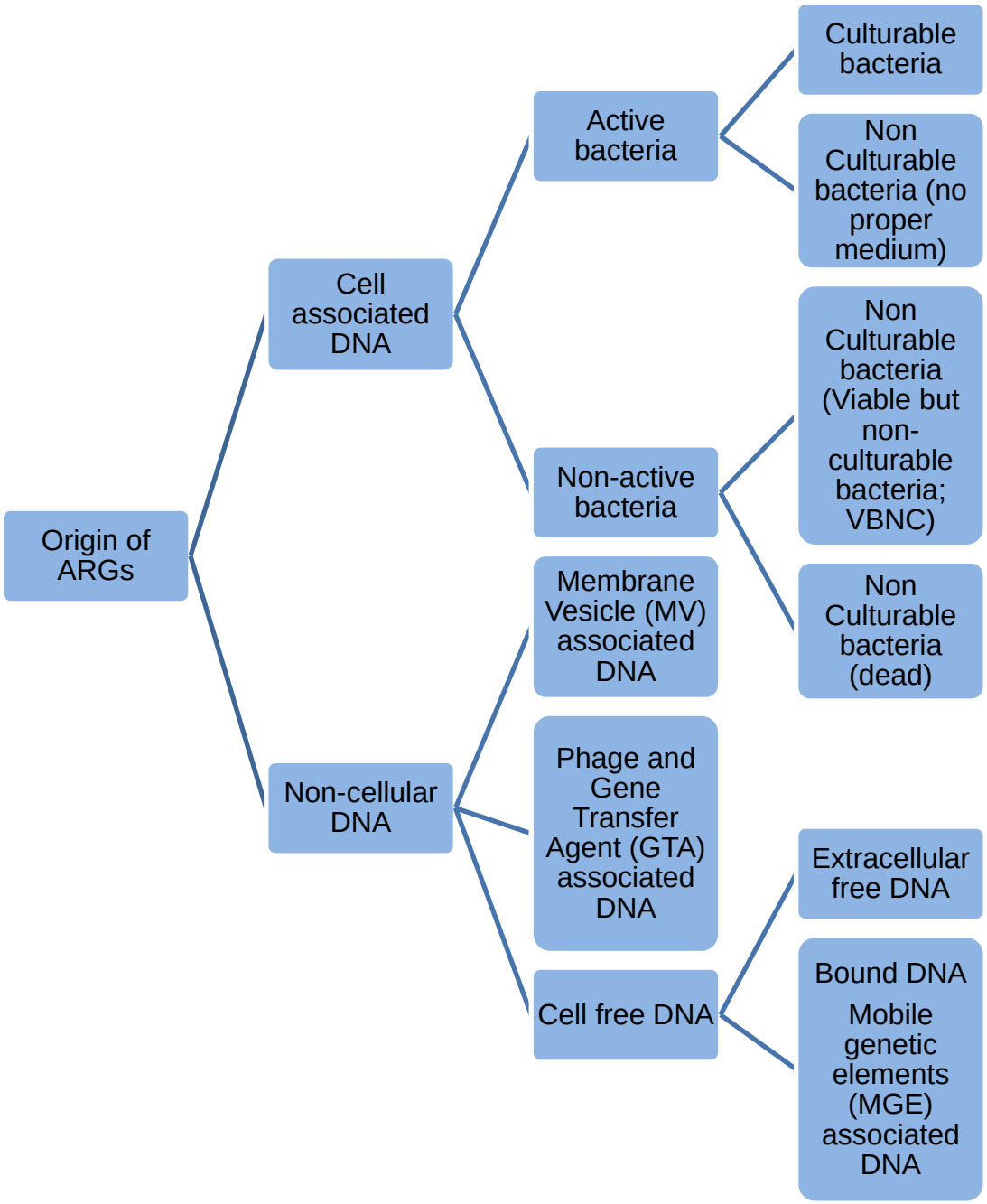

Figure 1. Forms and origins of ARGs quantified by molecular biology approaches (James *et al.*, 2021)

Regarding the published literature on the impact of biocides and/or heavy metals used in food animal production on the development of AMR, without prejudicing the findings of the proposed review, a preliminary scan of published data by the

applicants has immediately highlighted a number of issues that clearly need to be addressed in the full review.

Biocides

Essentially a biocide is defined as an active chemical molecule (agent) that controls the growth of, or kills, bacteria and other microorganisms in a biocidal product (SCENIHR, 2009; Wales & Davies, 2015; VKM, 2016). Biocidal substances act in different ways and sometimes several biocides are combined within a single product to increase the overall efficacy (VKM, 2016). Biocides are classified into different groups according to their application categories. Biocides used in food animal production operations are mainly disinfectants, sanitizing agents, or antiseptics, while biocidal preservatives may be used in animal feed (such as organic acids). As quoted in the FSA specification and numerous reviews (such as SCENIHR, 2009; VKM, 2016; Donaghy *et al.*, 2019) biocides are used for a number of reasons in animal production including, the cleaning and disinfecting of buildings as well as decontaminating ponds and equipment in fish farming. They are also used to create a barrier against bacteria and viruses by methods such as foot dips outside animal housing. They prevent infection when directly applied to animal skin, for example to clean udders of animals used for milk production and preserving specific products such as eggs or semen (SCENIHR, 2009; Donaghy *et al.*, 2019; VKM, 2016). Commonly used biocides in food animal production are: hydrogen peroxide, acetic acid, QACs, glutaraldehyde, formaldehyde, and isopropanol (VKM, 2016). While in aquaculture (fish farming) iodophores, metallic salts, halo-organic compounds, aldehydes, hydrogen peroxide, quaternary ammonium compounds and antimicrobial dyes are used (SCENIHR, 2009; VKM, 2016). Biocides are generally not used within body tissues (though some such as organic acids and essential oils have been added to animal feed and water as antimicrobial controls), but some, as already mentioned, (including alcohol, hydrogen peroxide, iodine, and trichlorophenols [TCP]) may be used on animal skin as antiseptics, for example to clean udders of animals used for milk production (Wales & Davies, 2015; VKM, 2016).

Biocidal products are controlled in Great Britain (England, Scotland and Wales) under the GB Biocidal Products Regulation (GB BPR) and in Northern Ireland under the EU Biocidal Products Regulation (EU BPR). A list of UK authorised biocidal products is provided by the HSE at https://www.hse.gov.uk/biocides/uk-authorised-biocidal-products.htm. Biocidal products used in food animal production on the basis of chemical group (McDonnell & Russell, 1999; SCENIHR, 2009; VKM, 2016) include:

- Antimicrobial dyes (Acridines, Triphenylmethane dyes, Quinones)
- Aldehydes
- Alcohols
- Anilides (such as Salicylanilide, Carbanilides)
- Biguanides (such as Chlorhexidine, Alexidine, Polymeric biguanides)
- Bromide
- Chlorine compounds (chlorine-releasing agents)
- Di-aminides
- Essential oils
- Iodine-releasing agents
- Organic and inorganic acids: esters and salts
- Peroxygens (such as Hydrogen peroxide, Peracetic acid, Ozone)
- Phenols
- QACs (quaternary ammonium compounds)

This review will focus on the impact of only biocides used in food animal production.

Heavy metals

Heavy metals are naturally occurring elements that have a high atomic weight and a density that is at least five (5) times greater than that of water. They can induce toxicity at low levels of exposure. The modes/mechanisms of action of heavy metals have been reviewed by Lemire *et al.* (2013). Due to the presence of heavy metals in the general environment, many bacteria have evolved mechanisms of metal tolerance. For any given metal, the toxicity varies widely, depending on the allotrope or oxidation state of the metal (VKM, 2016). Some metals are essential (Fe, I, Co, Zn, Cu, Mn, Mo, Se) to maintain various physiological functions and are usually added as nutritional additives in animal feed (Hejna *et al.*, 2018). Other uses include the application to livestock foot dips to treat skin problems such as dermatitis (Yu *et al.*, 2017) and wound dressings (Wales & Davies, 2015). Copper is also the principle biocidal component of anti-fouling paints used in aquaculture (Guardiola *et al.*, 2012). Heavy metals are often used in higher concentrations than needed to ensure adequate nutrition, therefore an excess may be excreted (Yu *et al.*, 2017). Other metals (Cd, F, Pb, Hg) have no established biological functions and are considered as contaminants/ undesirable substances (Hejna *et al.*, 2018). As requested in the FSA specification they will not be reviewed in this project. While arsenic (As) has been used in animal feeds and drugs in some countries (Silbergeld & Nachman, 2008; USFDA, 2021), it is not used in the UK and will not be included in this review. The use of silver (Ag) and zinc (Zn) nanoparticles as antimicrobial controls for a wide range of

applications, including in food animal production, have received considerable attention in recent years and will be included in this review.

There appears to be some evidence that heavy metals in certain forms may provide nutrition to food-producing animals but not be toxic to bacteria, and hence their use in feed would not co-select for resistance in bacteria (Yu *et al*., 2017). The strength of this evidence will be further reviewed in this project.

A suggested list of heavy metals that will be considered or excluded from this review are listed below; this will be formally agreed with the Agency at the start of the project:

Heavy metals	
Essential elements (Authorised in animal feed and drugs)	Non-essential elements (Undesirable)
cobalt (Co) copper (Cu) chromium (Cr) iron (Fe) manganese (Mn) molybdenum (Mo) selenium (Se) silver (Ag)* zinc (Zn)	arsenic (As) cadmium (Cd) mercury (Hg) lead (Pb)
To be included in review	To be excluded from review

* Antimicrobial control

Similarities and differences between antibiotic and biocide/heavy metal resistance

The following factors may influence the efficacy of antimicrobial agents and the resistance of bacteria to such agents (whether biocides and/or heavy metal) (SCENIHR, 2009; Wales & Davies, 2015; VKM, 2016):

- Innate resistance of bacteria
- Number and location of bacteria
- Age of bacterial community
- State: vegetative cells or spores
- Concentration and potency of the antimicrobial agent (low levels may still induce AMR)
- Physical and chemical factors (e.g., pH, temperature, salt, mode of application/contact)
- Organic and inorganic materials
- Duration of exposure (time)
- Attachment of bacteria and presence and state of biofilms

Role of biocides and/or heavy metals inducing AMR

Since biocides and their application are diverse so are the mechanisms of action of different biocides on bacteria and consequentially on AMR bacteria and their genes. As Wales & Davies (2015) note many biocides effect the membrane of bacteria, so Gram-negative bacteria are generally less susceptible to many biocides than Gram-positive bacteria. Unlike biocides, heavy metals are often used at inhibitory rather than lethal concentrations providing more potential for resistance to emerge (Wales & Davies, 2015).

The environmental persistence of biocides depends on the nature, action, and use of the biocide. While non-oxidising biocides (such as QACs) may persist in the environment (Wales & Davies, 2015), oxidising agents, (such as ozone, hydrogen peroxide, chlorine dioxide, sodium hypochlorite, peracetic acid and iodophors) by their nature are unstable and prone to degradation and rapidly breakdown. While many biocides breakdown during use, heavy metals are very persistent

and will accumulate in the environment. These biocidal substances, along with AMR bacteria and genes may be introduced into soil and water through sewage systems, direct excretion, land application of biosolids or animal manures as fertilisers, and irrigation with wastewater or treated effluents (Yazdankhah *et al.*, 2018). In England and Wales food animal production has been estimated to be a major source of environmental contamination by zinc and copper (Nicholson *et al.*, 2003, 2006).

There are a number of similarities and differences between antibiotic and biocide/heavy metal resistance (adapted from Weber *et al.*, 2019):

Similarities

Intrinsic resistance (e.g., spores are resistant to alcohols) and extrinsic resistance (e.g., efflux pumps for heavy metals) are well described.

Acquired mechanisms of resistance are similar (e.g., impermeability, efflux pumps).

Biofilms impair inactivation/killing.

Inactivation is dependent on the concentration and duration of contact with the antibiotic, biocide, or heavy metal.

Differences

Most antibiotics inhibit a specific target in a biosynthetic process.

Most biocides have multiple concentration-dependent targets, with subtle effects occurring at low concentrations and more damaging ones at higher concentrations.

There are some phenomena that confer reduced susceptibility both to antibiotics and to biocides and/or heavy metals (Wales & Davies, 2015; Donaghy *et al.*, 2019; Cheng *et al.*, 2019). These phenomena may be normally present (intrinsic) in the bacteria, or readily acquired by mutation or genetic transfer under appropriate conditions (Wales & Davies, 2015; Donaghy *et al.*, 2019). Phenomena such as spore formation, biofilm formation, nutrient stress responses, low cell wall permeability, and efflux pumps (transport proteins involved in the extrusion of toxic substrates from within cells into the external environment [Webber & Piddock, 2003]) are resistance mechanisms that may enable bacteria to resist antibiotics, biocides, and/or heavy metals (Wales & Davies, 2015; Donaghy *et al.*, 2019). Efflux pumps may expel a broad range of unrelated and structurally diverse compounds (including antibiotics, biocides, and/or heavy metals). Thus, whether intrinsic or acquired, bacteria possessing efflux pumps have substantial potential for cross-resistance to antibiotics, biocides, and/or heavy metals, though this does depend on the nature of the efflux pump (Webber & Piddock, 2003; Wales & Davies, 2015). Biofilms (complex structures formed by different or single types of bacteria adhering to surfaces) may enhance resistance to different agents. Biofilms have an extracellular matrix that provides a diffusion barrier and an enhanced medium for bacterial signalling and genetic exchange, plus a potential site for neutralisation or binding of chemical agents and an extracellular site for sequestration of metal ions (Wales & Davies, 2015; Donaghy *et al.*, 2019). Biofilms can also generate a state of hypermutability (capability for excessive mutation) that stimulates the development of resistance (Uruén *et al.*, 2021). Resistance may also be acquired through the release of resistance genes. They may potentially allow some proportion of the bacterial population to survive an otherwise terminal challenge, increasing the risk of selection of organisms permanently adapted to the antimicrobial agent (Wales & Davies, 2015). There can be a genetic link between resistance to different agents (co-resistance) through the co-location of resistance genes on mobile elements, such as plasmids and transposons (Bloomfield, 2002; Ciric *et al.*, 2011). Antibiotic resistance in many AMR bacteria is encoded by genes that are carried on large conjugative plasmids. These plasmids typically contain multiple ARGs as well as genes that confer resistance to biocides and/or heavy metals (Gulberg, 2014). An example of co-resistance are class 1 integrons, which encode a QAC efflux mechanism (*qacEΔ1*) plus sulphonamide resistance (*sul1*) and variable other antibiotic resistance genes (Carattoli *et al.*, 2001). Though resistance may be due to genetic linkage with resistance genes rather the efflux-mediated cross-resistance (Wales & Davies, 2015). However, an analysis of the co-occurrence of resistance genes to antibiotics, biocides, and metals by Pal *et al.* (2015) concluded that plasmids provide limited opportunities for biocides and metals to promote HGT of antibiotic resistance through co-selection (though this was more common in bacteria of animal origin), whereas ample possibilities exist for indirect selection via chromosomal biocide and metal resistant genes (BMRGs). The biocide/heavy metal may also influence genetic transfer. One study in particular has highlighted that while some biocides at a subinhibitory (residual) concentration may inhibit genetic transfer, others increase genetic transfer efficiency (Pearce *et al.*, 1999). Heavy metals have also been reported to facilitate HGT (Cheng *et al.*, 2019).

There is evidence that some adaptations that enable resistance to antimicrobial agents may result in associated costs to the organism (usually termed “fitness cost”). An example are broad substrate efflux pumps, which consume cell energy resources and indiscriminately remove some useful metabolic substances from the cell (Wales & Davies, 2015). Plasmids encoding resistance to biocides or heavy metals plus antibiotics have also been cited as another example (Gulberg *et al.*, 2014). However, some resistance adaptions, such as biofilms, may enhance survival in other environments (Wales &

Davies, 2015).

Thus there are two main types of related resistance:

> Cross-resistance - physiological adaptations that provide resistance to a number of toxic agents, examples being efflux pump upregulation, over expression or reduced cell wall/membrane permeability.
>
> Co-resistance – where resistance to different toxic agents is dissimilar but there is a genetic link between resistance to different agents, such as the co-location of different resistance genes on the same mobile element, such as plasmids. Because of the genetic linkage between the resistances, exposure to any of these groups of anti-microbials, or any combination of them, could co-select for the maintenance of the whole plasmid and all its associated resistances.

Cross-resistance and co-resistance are both co-selection mechanisms (Donaghy *et al.*, 2019).

As highlighted by Wales & Davies (2015), Cheng *et al.* (2019), Donaghy *et al.* (2019), and Giacometti *et al.* (2021) amongst others, while there is laboratory experimental evidence on the impact of biocides and/or heavy metals on antibiotic resistance there is considerably less field data. The efficacy of biocides in the field may be significantly reduced due to the presence of heavy organic soiling or dilution effects. Some examples of in field studies that have addressed the impact of biocides and/or heavy metals on antibiotic resistance that have been identified in our preliminary literature search are listed below (in chronological order):

Biocide/Heavy metal and AMR	Form of animal production	Reference
Biocide	Cattle (dairy)	Martin & Maris (1995)
Biocide	Poultry	Gradel *et al.* (2005)
Biocide	Cattle (dairy)	Randall *et al.* (2007)
Biocide	Pigs	Karatzas *et al.* (2007)
Biocide	Poultry	Peyrat *et al.* (2008)
Biocide	Poultry	Chuanchuen *et al.* (2008)
Biocide	Pigs	Chuanchuen *et al.* (2008)
Biocide	Pigs	Karatzas *et al.* (2008)
Heavy metal	Pigs	Aarestrup *et al.* (2010)
Biocide	Aquaculture	Stachowiak *et al.* (2010)
Heavy metal	Pigs	Cavaco *et al.* (2011)
Heavy metal	Cattle (veal calves)	Cavaco *et al.* (2011)
Heavy metal	Pigs	Slifierz *et al.* (2015)
Heavy metal	Pigs	Ciesinski *et al.* (2018)
Heavy metal	Pigs	Ghazisaeedi *et al.* (2020)
Biocide and heavy metal	Pigs	Puangseree *et al.* (2021)
Biocide	Poultry	Wang *et al.* (2021)
Heavy metal & biocide (essential oil)	Cattle	Murray *et al.* (2021)
Biocide and heavy metal	Poultry	Mustafa *et al.* (2021)
Biocide and heavy metal	Pigs	Mustafa *et al.* (2021)
Biocide	Poultry	Beier *et al.* (2021)
Heavy metal	Aquaculture	Ajewole *et al.* (2021)

An initial quick preliminary literature search has shown there to be few articles in relation to the impact of biocides and/or

heavy metals in aquaculture. There are also a number of studies that have addressed the impact of biocides and heavy metals on the transmission of AMR in manure and fertilisers of animal origin. These articles will be reviewed in detail in the project, as well as any other articles identified in the full in-depth literature search.

Hazard and risk

In considering the hazards and risks of the impact of biocide and/or heavy metal use during food animal production on AMR as with similar reviews (SCENIHR, 2009; VKM, 2016) the issue of the impact of biocides and/or heavy metals on AMR will be addressed either as a direct hazard or as an indirect hazard through resistance transfer.

- The direct hazard is the production of an antimicrobial resistant (pathogenic and commensal) bacterium.
- The indirect hazard arises through resistance transfer. In this case, the hazard is the transfer of resistance genes conferring resistance to antimicrobial agents (biocide, antibiotic, heavy metal) via mobile genetic elements (such as plasmids, transposons, etc) or other HGT routes to naturally susceptible bacteria.
- In some cases, both hazards may occur; a resistant bacterium may transfer an additional genetic element to another resistant bacterium, enhancing the resistance level.

The following definitions regarding the probability of biocides and/or heavy metals used in food animal production inducing AMR in food will be used (based upon the Biosafety Resource Book published by FAO in 2011 [Sensi *et al.*, 2011]) and as used in other reviews:

- Highly likely - is expected to occur in most circumstances
- Likely - could occur in many circumstances
- Unlikely - could occur in some circumstances
- Highly unlikely (effectively zero) - may occur only in very rare circumstances

This proposed review will help increase the Agency's understanding of whether, and to what extent the use of biocides and/or heavy metals in animal production leads to the development and spread of AMR within the food chain. Also, whether this could potentially lead to greater consumer exposure to AMR bacteria and genes from food, either directly through consumption of foods derived from animals that have been impacted by the use of biocides and/or heavy metals (e.g., the use of heavy metals in animal feed) or indirectly (e.g., exposure of crops to ARGs in fertiliser (manure) from food animal fed animal feed containing heavy metals).

How this proposal meets the FSA specification

The proposed study has been structured in line with the FSA specification and is squarely aimed at addressing all of the key elements requested in the FSA specification documents, namely the review will:

- Aim to identify and critically review what scientific evidence is available on the impact of biocides and/or heavy metals used in food animal production on the development of AMR.
- Gather and assess existing data in the literature (including peer-review journals, grey literature, and other sources) up to December 2022 (but will be flexible to extend that search end date should the publication of the final report be delayed).
- Address the following key questions/points (terms of reference) cited in the FSA specification, namely:
    - Is there evidence to show that biocides and/or heavy metals used in food animal production have an impact on the development of AMR?
    - How long are biocides and/or heavy metals (used in food animal production) able to persist in the animal production environments and how does this impact on the development of AMR and associated risks?
    - What evidence is there that biocide and/or heavy metal associated AMR enters the food chain through products of animal origin or as a result of crop contamination?
    - Is there a potential risk to the consumer from AMR acquired through the use of biocides and/or heavy metals in food animal production?

To ensure that the review is both transparent and reproducible a list of all the databases and key search terms used will be documented as well as any indicative criteria for inclusion and rejection based on the quality of the studies being considered. Finalised key search terms will be agreed with the Agency prior to project initiation. A full database of all the relevant articles will be provided to the Agency. The database will be in a format suitable for publication on the FSA website e.g., in an accessible format (for example CSV or Excel).

The proposed study has been structured in line with the specification and is squarely aimed at addressing all of these key

elements. If other elements not listed are identified as being significant regarding the impact of biocides and/or heavy metals on AMR bacteria/genes during the review these will be discussed with the Agency and incorporated into the work programme, if considered appropriate.

The project team will work closely with Agency representatives throughout the agreed timeline and monitor progress of the project to ensure the maximum visibility and usability of all findings and dissemination materials produced by the project.

Proposed scientific approach

The proposed work will carry out a broad critical review of the available scientific literature to assess the impact of biocides and/or heavy metals used in food animal production on the development of AMR.

The project will be carried out by a project team from the Food Refrigeration & Process Engineering Research Centre (FRPERC) at the Grimsby Institute of Further and Higher Education (GIFHE), part of the TEC Partnership; the University of Lincoln; the University of Liverpool. The project team has extensive experience and expertise in the food chains operations from farm-to-fork, having, in their time, carried out studies on the control of microbial hazards (including AMR) at all stages from the farm to the home. The staff who will be working on this project all have experience and a long track record of designing and carrying out similar critical literature reviews of relevant scientific literature (including for the Agency) and among them have practical experience and expertise of AMR, bacteriology, and PCR based techniques. The team's recent review for the Agency (Assessing the impact of heat treatment of food on antimicrobial resistance genes and their potential uptake by other bacteria) covered reviewing current knowledge on AMR gene transfer mechanisms and pathways. They are thus ideally placed to ensure that the findings of this review are robust and relevant to practices used in the UK and to the needs of the key stakeholders.

Examples of reviews (or projects including reviews of scientific literature) that they have led or been involved, since 2000, include:

- James, C., Purnell, G., & James, S. J. (2003). Review of the use of ozone in red meat and poultry processing. Food Standards Agency (FSA) project no. ZM0104.
- James, C., James, S. J., & Buncic, S. (2004). Review of potential effects of transporting meat above 7°C. Food Standards Agency (FSA) project no. ZM01011.
- James, C., Pinho, R. M., & James, S. J. (2006). Safety implications of the manufacture of minced meat from aged meat. Food Standards Agency (FSA).
- James, C., Vincent, C., de Andrade Lima, T. I., & James, S. J. (2006). The primary chilling of poultry carcasses – a review. *International Journal of Refrigeration*, 29:6, 847-862.
- Newell, D. G., Allen, V., Elvers, K., Dorfper, D., Hanssen, I, Jones, P., James, S., Gittins, J., Stern, N., Davies, R., Connerton, I., Pearson, D., & Salvat, G. (2008). B15025: A critical review of interventions and strategies (both biosecurity and non-biosecurity) to reduce Campylobacter on the poultry farm. Food Standards Agency (FSA) project no. B15025.
- James, C., Purnell, G., & James, S. J. (2013). Description of the processes used in the UK to manufacture MSM and former DSM meat products from poultry and pork and an initial assessment of microbiological risk. Food Standards Agency (FSA) project no. FS503001.
- James, C., Derrick, S., Purnell, G., & James, S. J. (2013). Review of the risk management practices employed throughout the fish processing chain in relation to controlling histamine formation in at-risk fish species. Food Standards Agency (FSA) project no. FS241055.
- James, C., Daramola, B., Dudkiewicz, A., Reyers, F., Purnell, G., Turner, R., James, S. J., & Braybrooks, V. (2014). Qualitative Risk Assessment to support a policy decision on partially-eviscerated (effilé) poultry production. Food Standards Agency (FSA) project no. FS101044.
- James, C., Purnell, G., & James, S. J. (2015). A review of novel and innovative freezing technologies. *Food and Bioprocess Technology*, 8, 1616-1634.
- James, C., Onarinde, B. A., & James, S. J. (2017). The use and performance of household refrigerators: A review. *Comprehensive Reviews in Food Science and Food Safety*, 16(1), 160–179.
- James, C., Daramola, B., Chu, J., Dudkiewicz, A., Purnell, G., & James, S. J. (2018). Exploring the potential for technology to support agency objectives in meat operations. Food Standards Agency (FSA) project no. SEP-EOI-02.
- James, C., Dixon, R. A., Talbot, L., James, S. J., Williams, N., Onarinde, B. A. (2021). Assessing the impact of heat treatment on antimicrobial resistance genes and their potential uptake by other 'live' bacteria. Food Standards Agency (FSA) project no. FS307036.

- James, C., Dixon, R., Talbot, L., James, S. J., Williams, N., & Onarinde, B. A. (2021). Assessing the impact of heat treatment of food on antimicrobial resistance genes and their potential uptake by other bacteria - A critical review. *Antibiotics*, 10(12) p1440. doi.org/10.3390/antibiotics10121440.

A mixed-method knowledge synthesis approach will be adopted for this critical review, based on the approaches used by Newell *et al.*, (2008), Mateus *et al.* (2016), Hutchison *et al.* (2020), EFSA BIOHAZ Panel (2021), James *et al.* (2021) amongst others. This should enable a critical review to be completed that is as unbiased, and as evidence-based as possible. The use of a structured and transparent approach to identify, assess, and synthesize available evidence on the impact of biocides and/or heavy metals used in food animal production on the development of AMR should provide more credible and reliable evidence to the Agency than a traditional narrative review. Although it is anticipated that the review will incorporate traditional narrative aspects where appropriate (e.g., when highlighting data gaps, and identifying, highlighting, and recommending areas for further work). The approach will follow that detailed in the Agency's specification, i.e.:

- The review will adopt a comprehensive search strategy considering all available evidence in the public domain, including peer-reviewed articles, grey literature (e.g., government and industry reports), relevant government reports (e.g., FSA published studies, ACMSF reports, etc.), European and International literature (e.g., the EFSA Scientific Opinions, WHO reports) up to December 2022. This will include previously published systematic and critical reviews, and risk assessments, as well as primary research.
- The proposal lists the databases and key search terms to be used and also any indicative criteria for inclusion and rejection based on the quality of the studies being considered. Finalised terms will be agreed with the Agency prior to project initiation.
- The review will focus on identifying and reviewing both quantitative and qualitative information on the impact of biocides and/or heavy metals used in food animal production on the development of AMR. The criteria for selection and non-selection of relevant information for consideration in the review will be agreed with the Agency and included in the final report.

The project has five objectives:

- Objective 1: Literature search: To carry out a structured literature search of appropriate bibliographic databases and sources in order to compile a broad data set of as many potentially relevant articles.
- Objective 2: Article screening: To screen the compiled data set of potentially relevant articles in order to select important articles for data extraction.
- Objective 3: Data extraction and analysis: To extract, and analyse, pertinent data from the articles that have been selected as clearly relevant.
- Objective 4: Data synthesis and review completion: To synthesise the extracted data from articles into a formal review report in order to establish what existing data and understanding there is on the impact of biocides and/or heavy metals used in food animal production on the development of AMR.
- Objective 5: Dissemination: To disseminate the findings of the project to key stakeholders to inform them of what realistic actions are required to reduce the risks associated with biocides and/or heavy metals used in food animal production on the development of AMR and where further work is required.

To realise **Objective 1**, the **literature search**, the project will follow the following key approaches.

It is proposed that the review question will be:

"Do biocides and/or heavy metals used in food animal production have an impact on the development of AMR in the food chain?"

The key elements of the question (PIO): Population (P), Intervention (I), and Outcome (O) are:

- The **population** of interest will include pathogenic and non-pathogenic AMR bacteria and their resistance genes. But will exclude microorganisms other than bacteria, such as viruses, fungi, and parasites.
- All biocide or heavy metal **interventions** used in food animal production.
- Relevant **outcome measures** for interventions are what impact does the intervention have on AMR bacteria and AMR genes and resistance.

All AMR bacteria and genes of immediate or emerging concern will be considered. A search for specific AMR genes will not be carried out in the initial literature search, since there are so many of potential concern, some with rapid mechanisms for transfer. The review will focus on critically important AMR genes, using the WHO list of critically important antimicrobials

for human medicine (WHO, 2019) as a reference.

Initial Consultation

Before commencing the literature search, the review question, keywords, scope of search, and eligibility criteria will be agreed with the Agency. Suggested keywords, scope of search, and eligibility criteria are listed below.

Inclusion/Exclusion Criteria

All evidence on the impact of biocides and/or heavy metals used in food animal production on the development of AMR available in the public domain will be considered, including primary research, previously published reviews, and risk assessments. The literature search will be restricted to English-language peer-reviewed journals, books, reports, or articles. Grey literature (e.g., government and industry reports) will also be considered. The results will be refined by relevance to keywords. Post-2000 articles will be given precedence, but older articles may be considered for background information.

Search Engines/Databases

The following databases / search engines will be used:

- Web of Science from 1990-current
- MEDLINE from 1990-current
- Scopus from 1990-current
- Google Scholar from 1990-current

If any other relevant databases are identified in the early stages of the project, these will be considered and include if agreed of importance by the project team and FSA Project Officer. Inclusion of the following databases / search engines will be considered:

- PubMed.Net from 1990–current
- EMBASE from 1990-current
- CAB abstracts from 1990-current
- ScienceDirect from 1990-current
- Biomed Central from 1990-current
- Food Science and Technology abstracts from 1990-current

The bibliographic databases to be used include food production, agriculture, public health, and food safety subject areas. In addition, search verification will be conducted by reviewing a reference list of a selection of relevant original research, review articles and book chapters.

Supplementary Collation Methods

In addition to the database searches, collation will be supplemented by:

- Searching through relevant government reports, e.g., FSA published studies, ACMSF reports, etc.
- European and International literature, e.g., EFSA scientific opinions, WHO reports, etc.
- Searching of key journals, e.g., International Journal of Food Microbiology, Journal of Food Protection, etc.
- Searching articles, e.g., Environmental Health News Magazine/Online.
- Contacting experts.
- Reference list tracking, Reference lists of all studies selected for inclusion will be searched to identify further relevant studies.
- A public “call for data”.

Keywords and search string, and Boolean operators

Finalised keywords will be agreed with the Agency prior to project initiation. Suggested categorised search words are:

1	2	3
co-selection antimicrobial resistance antimicrobial resistant antibiotic resistance antibiotic resistant drug resistant drug resistance multidrug resistant	antiseptic biocide* disinfectant* sanitizer* sanitiser* essential oil* heavy metal* antifouling	"food animal production" fish seafood aquaculture salmon trout cow cattle

multidrug resistance multi resistance multi resistant ABR AMR MDR MAR AMRG		dairy pig swine sheep lamb poultry chicken turkey livestock food manure slurry fertiliser feed crop* “ground water” soil

For full Boolean search, a full suggested search string is:

(co-selection OR "antimicrobial resistance" OR "antimicrobial resistant" OR "antibiotic resistance" OR "antibiotic resistant" OR "drug resistant" OR "drug resistance" OR "multidrug resistant" OR "multidrug resistance" OR "multi resistance" OR "multi resistant" OR ABR OR AMR OR MDR OR MAR OR AMRG) AND (antiseptic OR biocide* OR disinfectant* OR sanitizer* OR sanitiser* OR "essential oil*" OR “heavy metal*" OR antifouling) AND ("food animal production" OR fish OR seafood OR aquaculture OR salmon OR trout OR cow OR cattle OR dairy OR pig OR swine OR sheep OR lamb OR poultry OR chicken OR turkey OR livestock OR food OR manure OR fertiliser OR feed OR crop* OR “ground water” OR soil)

The search algorithm has been pre-tested in Web of Science and identified 2,543 articles for initial screening.

For databases that limit the size of search string the most relevant keywords from the first and the second category will be combined with one of the keywords of categories 3.

Any searches of the literature and criteria used will be documented at all times to allow replication of the methodology used.

Collation of articles

For all searches, citations and abstracts will be uploaded from each of the electronic databases into Covidence [https://www.covidence.org] (this SR tool has been chosen because a number of reviews of SR tools (Kellermeyer *et al.*, 2018; Van der Mierden *et al.*, 2019; Harrison *et al.*, 2020) have highlighted it as the most comprehensive SR tool package and one of the most easy to use). The applicants have used Covidence on a previous similar AMR critical review project (FS307036) for the Agency. The references will be processed using the ‘find duplicates’ automated functionality of the program and the duplicates will be removed.

To ensure that all of the pertinent articles are identified, the search strategy will be verified by checking the generated list of references against the cited reference lists of a random selection of five articles for all searches. To ensure completely random selection of articles, the articles will be sorted by author name and each assigned a sequential number. The ‘cited by’ functionality of the Web of Science will be used to identify that those articles published after the five randomly-selected references, which cited these articles, have been included in the search-generated reference list.

Objective 1 will produce a database consisting of collated citations and abstracts of all articles identified in the literature search.

To realise **Objective 2**, **article screening**, the project will follow the following key approaches.

Selection of articles for data extraction

The relevance of each unique citation/article will be assessed at the title and abstract level within Covidence. Abstracts will be excluded if:

- They contain no relevant data on the impact of biocides and/or heavy metals used in food animal production on the development of AMR.

- Articles describing development of resistance in microorganisms other than bacteria, such as viruses, fungi, and parasites.
- Are in a language other than English.
- Measure irrelevant population (viruses, fungi, and parasites), interventions (biocide not used in food animal production [for example, healthcare]; used for their surfactant properties, antimicrobial peptides [for instance, bacteriocins]; or undesirable heavy metals (such as arsenic [As], cadmium [Cd], mercury [Hg], lead [Pb]), outcomes (does not include impact on AMR bacteria or genes).

The criteria will be independently applied to the abstract of each paper by at least two members of the project team. For each citation, a consensus will be reached that the article is relevant for inclusion. Arbitration by a third member of the project team will be used to settle conflicting appraisals. Full articles will be obtained for all abstracts that pass the inclusion criteria. To ensure transparency a record will be kept of all articles determined as not relevant.

A preliminary search of articles on the impact of biocides and/or heavy metals used in food animal production on the development of AMR (using the suggested keyword search) has shown that the initial broad literature search will identify a large number (1661 in Web of Science) of complex and diverse articles that may be relevant. However, having looked through a sub-section of the abstracts that this preliminary broad search identified it is expected that articles specifically related to the impact of biocides and/or heavy metals used in food animal production on the development of AMR will possibly only number in the low hundreds at most. At present 75 potentially relevant full articles have been collected during the production of this tender. In order to prevent data saturation without analysing all captured articles in detail, we will prioritize the selection of articles. Our criteria for prioritization will include the following: (1) unique or comprehensive insights are provided, (2) article is broadly applicable and generalizable, and (3) sufficient information is reported for extraction.

Objective 2 will produce a database consisting of collated citations and abstracts of (1) all articles identified in the literature search, and (2) screened articles considered of direct relevance to the overall objectives of the project. This database will also provide the criteria used for the selection and non-selection of relevant articles.

Mid-point interim review. In Month 3 a mid-point interim report will be produced for the Project Officer that will report on project progress across both Objectives and all Tasks. The purpose of the review will be to assist the Agency and the team to review and assess the progress made to date against the project's technical objectives and its contractual targets and to determine whether any remedial action is necessary to bring a project back on track or agree any changes to the project's remaining objectives and deliverables in the light of work already undertaken.

To realise **Objective 3**, **data extraction and analysis**, data from the articles identified, screened, and collated as relevant in Objective 2 will be extracted and analysed by the project team as per the following key approaches.

Data extraction and analysis of relevant literature

Once collected, the relevance of each unique article will be assessed again at the full article level again within Covidence to ensure the relevance of the article. For each article identified in the initial screening as relevant, two of the team will read the entire paper. If considered relevant, an in-depth content analysis of the selected articles will be carried out. Each will extract the key elements of interest from each paper. These will be collated by the PI and used to produce the draft critical review of the literature. The complied draft critical review will then be reviewed by the entire project team, with the final editing carried out by the PI before submission to the FSA Project Officer.

The reviewers will assess what existing data there is in the literature that addresses the following key questions/points:

- Is there evidence to show that biocides and/or heavy metals used in food animal production have an impact on the development of AMR?
- How long are biocides and/or heavy metals (used in food animal production) able to persist in animal production environments and how does this impact on the development of AMR and associated risks?
- What evidence is there that biocide and/or heavy metal associated AMR enters the food chain through products of animal origin or as a result of crop contamination?
- Is there a potential risk to the consumer from AMR acquired through the use of biocides and/or heavy metals in food animal production?

A template for data extraction will be prepared by the research team based on the PIO (Population, Intervention and Outcome(s)) as an Excel document. This template will be tested prior to implementation. Once implemented, the template will be used by reviewers to collect the data from eligible studies. Study characteristics (e.g., study design, sample size,

sampling methods amongst others) and outcome(s) of interest will be described and summarised accordingly.

The uncertainty in this review will be investigated in a qualitative manner following the procedure detailed in the EFSA guidance on uncertainty analysis in scientific assessments (EFSA Scientific Committee, 2018a,b). The sources of the main uncertainties will be identified and for each of these the nature or cause of the uncertainties described. Expert judgement will be used to estimate the individual impact of each of the uncertainties on the possible role played by the use of biocide and/or heavy metal use in food animal production on the emergence and transfer of AMR and on the general conclusions

Objective 3 will produce a database consisting of the key data extracted from articles of direct relevance to the overall objectives of the project.

To realise **Objective 4**, **Data synthesis and review completion**, the data extracted and analysed from individual articles in Objective 3 will be synthesised and reviewed by the project team and a formal technical report completed, as per the following key approaches.

Data synthesis and report completion

To synthesise the data extracted and evaluate its quality a narrative approach will be used. This will be used to; a) develop a synthesis of findings of the studies, b) investigate relationships within and between studies, and c), evaluate the degree of robustness of the synthesis. The findings of the review will be collected in a technical report suitable for publication on the FSA website and structured and formatted in accordance with guidelines from the FSA Web Content Accessibility Guidelines (the applicants are fully aware of these guidelines and have full experience of having previously produced a report for the Agency meeting these guidelines [*Assessing the impact of heat treatment on antimicrobial resistance genes and their potential uptake by other 'live' bacteria*, FS307036.]). A database of the articles included in the review will also be provided. The database will be in a format suitable for publication on the FSA website. The technical report will identify the impact of biocides and/or heavy metals used in food animal production on the development of AMR. The report will also highlight any information gaps and identify and recommend areas for further work.

A draft final report will be submitted at least 4 weeks before the final report is due to allow time for Agency officials to provide comments.

Objective 4 will produce a report that will include a lay summary, executive summary, introduction (including the background and aims/objectives of the study), methodology, and key findings of the review, discussions, conclusions, what remains unknown, uncertainty around findings, and recommendations for further work. The criteria for selection and non-selection of articles relevant for consideration in the review will also be clearly identified in the report. The report will be suitable for publication on the FSA website and structured and formatted in accordance with guidelines from the FSA Web Content Accessibility Guidelines

To realise **Objective 5**, **Dissemination**, a full dissemination and exploitation plan will be agreed with the FSA Project Officer during the project.

Following completion of the final report, a meeting will be held with FSA officials after completion of the final report to discuss the key project findings and recommendations arising from the review. In addition to the final report the findings of the project will be disseminated to key stakeholders in the form of a scientific paper (with the approval of the funder) and presentations. Example dissemination activities may include:

1. An executive summary document / press release agreed with the Agency and distributed to key stakeholders.
2. At least one key paper will be submitted on “A comprehensive critical review of the impact of biocides and/or heavy metals used in food animal production on the development of AMR” for consideration for publication in a suitable peer-reviewed open access journal, such as Antibiotics.
3. The presentation of results to a FSA review panel and at any FSA conference, workshop, seminar, or related event, as required by the Agency.
4. Presenting, or supporting the presentation, of the findings of this work at a future FSA AMR ‘show and tell’ event, ACMSF (or AMR sub-group) meetings, and at stakeholder meetings if needed.
5. Assisting the FSA in producing documents involved in the publication of the study findings which will include a Q&A document and providing comments on news story.
6. Presentation of the study at the FSA’s AMR R&E Programme Review on 8th and 9th November 2022.

7. Presentation of key findings from the study to be given to the ACMSF working group on AMR in early 2023 (FSA to confirm date in due course but likely to be in either January or February 2023).

Timeframe: The proposed review will take 8 months to complete.

Key project outcomes/deliverables

This proposed review will help increase the Agency's understanding of AMR risks arising as a consequence of using biocides and certain heavy metals in food animal production. It will:

1. Enable an understanding of which specific risks should be targeted to reduce the transmission pathway of AMR to humans arising as a consequence of using biocides and certain heavy metals in food animal production and identify where the knowledge gaps for further interventions and research/surveillance are required. It will provide robust, evidence-based analysis of the impact of using biocides and certain heavy metals in food animal production on the survival and transmission of AMR bacteria and AMR genes and the extent to which biocides and/or heavy metals give rise to the selection and spread of AMR bacteria into the food chain and make recommendations for any further work required to reduce the impact of these compounds on AMR.
2. Provide a review that will be used to inform measurable progress towards developing interventions and research/surveillance that will protect consumers from the risks associated with AMR and AMR genes as a consequence of using biocides and certain heavy metals in food animal production.
3. Provide findings that will help the agency achieve its main aim of protecting public health from all potential risks which may arise in connection with the consumption of food.
4. Provide a report that will be used to inform key stakeholder what realistic actions are required to reduce the risks associated with AMR in food animal production and make a timely positive contribution to the cross-governmental objective of protecting consumers from the risks associated with AMR and AMR genes.

Key outcomes/deliverables will be:

- A full technical report addressing the relevant areas of the study in a format suitable for publication on the Agency website, structured and formatted in accordance with guidelines from the FSA Web Content Accessibility Guidelines. The report will include a lay summary, executive summary, introduction (including the background and aims/objectives of the research), methodology, findings, discussions (including the limitations of the models created), conclusions, references, and recommendations for further work.
- Full details of the data collected will be provided in a systemised format and a library of references organised using an appropriate reference management system.
- Publication of research findings in peer reviewed open access literature and presentations at scientific conferences. Such material will be submitted to the Agency for approval prior to submission.
- A meeting with Agency officials to discuss the project findings and active support in subsequent dissemination of the findings.

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B. INNOVATION

Please provide details of any aspect of the proposed work which are considered innovative in design and/or application? E.g. Introduction of new or significant improved products, services, methods, processes, markets and forms of organization.

The approach taken by this project will be based on firm established methods for carrying out a critical review of published literature so will not be fundamentally innovative. It will however differ from recent reviews on this topic by trying to clearly identify and highlight what clear evidence there is in the scientific literature on the AMR hazards and risks arising as a consequence of biocide and/or heavy metal use in food animal production and any potential risk to the consumer from AMR acquired through the use of biocides and/or heavy metals in food animal production, what evidence gaps remain, and recommend how those gaps may be addressed. While published reviews appear to have identified and reviewed how this may be a potential risk, they appear less clear in establishing how many in field studies have been carried out and what they have found.

3: THE PROJECT PLAN AND DELIVERABLES

A. The Plan

Please provide a detailed project plan including, the tasks and sub-tasks required to realise the objectives (detailed in Part 1). The tasks should be numbered in the same way as the objectives and should be clearly linked to each of the objectives. Please also attach a flow chart illustrating the proposed plan.

The following work programme will commence on the 1st of August 2022 in line with the tender specification provided.

The project has been structured to look at the key interactions in a methodical but cost-effective manner. Work on some Objectives and Tasks will be carried out in parallel, using material produced in other Tasks.

It is proposed that the review question will be: "Do biocides and/or heavy metals used in food animal production have an impact on the development of AMR in the food chain?"

The key elements of the question (PIO): Population (P), Intervention (I), and Outcome (O) are:

- The **population** of interest will include pathogenic and non-pathogenic AMR bacteria and their resistance genes . But will exclude microorganisms other than bacteria, such as viruses, fungi, and parasites
- All biocide or heavy metal **interventions** used in food animal production.
- Relevant **outcome measures** for interventions are what impact does the intervention have on AMR bacteria and AMR genes and resistance.

Objective 1: Literature search – Identification and collection of articles that may contain relevant evidence on the impact of biocides and/or heavy metals used in food animal production on the development of AMR

Timescale: Months 1 to 3 (and a revisit in Months 6 to 7)

Staff: All of the project team.

Task 1.1: Agreement of review question, keywords, scope, and eligibility criteria (Month 1)

The review question, keywords, scope of search, and eligibility criteria will be agreed with the Agency following consultation, before commencing the literature search.

Task 1.2: Literature search (Months 1 to 3)

Searches of the bibliographic databases will be carried out, using keywords agreed with the Agency.

The following databases / search engines will be used:

- Web of Science from 1990-current
- MEDLINE from 1990-current
- Scopus from 1990-current
- Google Scholar from 1990-current

Inclusion of the following databases / search engines will be considered:

- PubMed.Net from 1990–current
- EMBASE from 1990-current
- CAB abstracts from 1990-current
- ScienceDirect from 1990-current
- Biomed Central from 1990-current
- Food Science and Technology abstracts from 1990-current

In addition to the database searches, collation will be supplemented by:

- Searching through relevant government reports, e.g. FSA published studies, ACMSF reports, etc.
- European and International literature, e.g. EFSA scientific opinions, WHO reports, etc.
- Searching of key journals, e.g. International Journal of Food Microbiology, Journal of Food Protection, etc.
- Searching articles, e.g. Environmental Health News Magazine/Online.
- Contacting experts.
- Reference list tracking, Reference lists of all studies selected for inclusion will be searched to identify further relevant studies.
- A public “call for data”.

Finalised keywords will be agreed with the Agency prior to project initiation. Suggested categorised search words are:

1	2	3
co-selection antimicrobial resistance antimicrobial resistant antibiotic resistance antibiotic resistant drug resistant drug resistance multidrug resistant multidrug resistance multi resistance multi resistant ABR AMR MDR MAR AMRG	antiseptic biocide* disinfectant* sanitizer* sanitiser* essential oil* heavy metal* antifouling	"food animal production" fish seafood aquaculture salmon trout cow cattle dairy pig swine sheep lamb poultry chicken turkey livestock food manure slurry fertiliser feed

		crop* “ground water” soil

For Boolean search, a full suggested search string is:

(co-selection OR "antimicrobial resistance" OR "antimicrobial resistant" OR"antibiotic resistance" OR "antibiotic resistant" OR "drug resistant" OR "drug resistance" OR "multidrug resistant" OR "multidrug resistance" OR "multi resistance" OR "multi resistant" OR ABR OR AMR OR MDR OR MAR OR AMRG) AND (antiseptic OR biocide* OR disinfectant* OR sanitizer* OR sanitiser* OR "essential oil*" OR “heavy metal*" OR antifouling) AND ("food animal production" OR fish OR seafood OR aquaculture OR salmon OR trout OR cow OR cattle OR dairy OR pig OR swine OR sheep OR lamb OR poultry OR chicken OR turkey OR livestock OR food OR manure OR fertiliser OR feed OR crop* OR “ground water” OR soil)

For databases that limit the size of search string the most relevant keywords from the first and the second category will be combined with one of the keywords of categories 3.

Any searches of the literature and criteria used will be documented at all times to allow replication of the methodology used.

To ensure that all the pertinent articles are identified, the search strategy will be verified by checking the generated list of articles against the cited reference lists of a random selection of five articles for all searches. The ‘cited by’ functionality of the Web of Science will then be used to identify those articles published after the five randomly-selected references, which cited these articles, have been included in the search-generated reference list.

During this reviewing process individual authors or research teams carrying out very relevant work will be identified. These authors will be contacted directly to ask whether they know of any other published or unpublished studies of direct relevance to the project.

Task 1.3: Collation of articles

For all searches, citations and abstracts will be uploaded from each of the electronic databases into Covidence. The references will be processed using the ‘find duplicates’ automated functionality of the program and the duplicates will be removed.

Task 1.4: Revisit (Months 6 and 7)

In the penultimate month of the project the literature search will be performed again to identify if any new relevant articles have been published during the course of the project. Any articles identified will identified, screened, and reviewed in the same manner as previous articles, and if relevant incorporated into the final report.

Milestones and Deliverables:

M1: Before commencing the literature search, the review question, keywords, scope of search, and eligibility criteria will be agreed with the Agency (Task 1.1).

D1: Database of initial results of literature search - collated citations and abstracts (results of Task 1.3).

See Gantt and Deliverables table for further information.

Objective 2: Article screening – Selection of articles with relevant data on the impact of heat treatment of food on AMR genes

Timescale: Month 3

Staff: All of the project team.

Task 2.1: Selection of articles for data extraction

The relevance of each unique citation/article will be assessed at the title and abstract level within Covidence. Abstracts will be excluded if:

- They contain no relevant data on the impact of biocides and/or heavy metals used in food animal production on the development of AMR.
- Articles describing development of resistance in microorganisms other than bacteria, such as viruses, fungi, and parasites.

- Are in a language other than English.
- Measure irrelevant population (viruses, fungi, and parasites), interventions (biocide not used in food animal production [for example, healthcare]; used for their surfactant properties, antimicrobial peptides [for instance, bacteriocins]; or undesirable heavy metals (such as arsenic [As], cadmium [Cd], mercury [Hg], lead [Pb]), outcomes (does not include impact on AMR bacteria or genes).

The criteria will be independently applied to the abstract of each paper by at least two members of the project team. For each citation, a consensus will be reached that the citation is relevant for inclusion. Arbitration by a third member of the project team will be used to settle conflicting appraisals. Full articles will be obtained for all abstracts that pass the inclusion criteria. To ensure transparency a record will be kept of all articles determined as not relevant.

Milestones and Deliverables:

M2: Initial literature search and screening completed (Objective 2 complete).

D2: Screened database of relevant collated citations and abstracts (results of Task 2.1).

See Gantt and Deliverables table for further information.

Mid-point interim review (Month 4)

In Month 3 a mid-point interim report will be produced for the Project Officer that will report on project progress across both Objectives and all Tasks.

Milestones and Deliverables:

D3: Mid-point interim project progress report

Objective 3: Data extraction and analysis - extraction of relevant evidence on the impact of biocides and/or heavy metals used in food animal production on the development of AMR

Time scale: Months 3 to 5.

Staff: All of the project team.

Task 4.1: Data extraction from relevant articles and analysis

When extracting data from the individual screened articles, the reviewers will bear in mind the review question, i.e. “Do biocides and/or heavy metals used in food animal production have an impact on the development of AMR in the food chain?”

Once collected, the relevance of each unique article will be assessed again at the full article level again within Covidence to ensure only relevant articles are considered. For each article identified in the initial screening as relevant, two of the team will read the entire paper. If considered relevant, n in-depth content analysis of the selected articles will be carried out. For each article identified as relevant, two of the team will read the entire paper. Each will extract the key elements of interest from each article.

The reviewers will assess what existing data is there in the literature that addresses the following key questions/points:

- Is there evidence to show that biocides and/or heavy metals used in food animal production have an impact on the development of AMR?
- How long are biocides and/or heavy metals (used in food animal production) able to persist in animal production environments and how does this impact on the development of AMR and associated risks?
- What evidence is there that biocide and/or heavy metal associated AMR enters the food chain through products of animal origin or as a result of crop contamination?
- Is there a potential risk to the consumer from AMR acquired through the use of biocides and/or heavy metals in food animal production?

A template for data extraction will be prepared by the research team based on the PIO (Population, Intervention and Outcome(s)) as an Excel document. This template will be tested prior to implementation. Once implemented, the template will be used by reviewers to collect the data from eligible studies. Study characteristics (e.g., study design, sample size, sampling methods amongst others) and outcome(s) of interest will be described and summarised accordingly.

The uncertainty in this review will be investigated in a qualitative manner following the procedure detailed in the EFSA guidance on uncertainty analysis in scientific assessments (EFSA Scientific Committee, 2018a,b). The sources of the

main uncertainties will be identified and for each of these the nature or cause of the uncertainties described. Expert judgement will be used to estimate the individual impact of each of the uncertainties on the possible role played by the use of biocide and/or heavy metal use in food animal production on the emergence and transfer of AMR and on the general conclusions

Deliverables:

M3: Data extraction and analysis of articles completed (Task 3.1 complete).

Objective 4: Data synthesis and report completion – review of published literature on evidence on the impact of biocides and/or heavy metals used in food animal production on the development of AMR

Timescale: Months 6 to 8

Staff: All of the project team.

To synthesise the data extracted and evaluate its quality a narrative approach will be used. This will be used to; a) develop a synthesis of findings of the studies, b) investigate relationships within and between studies, and c), evaluate the degree of robustness of the synthesis. The findings of the review will be collected in a technical report suitable for publication on the FSA website and structured and formatted in accordance with guidelines from the FSA Web Content Accessibility Guidelines (the applicants are fully aware of these guidelines and have full experience of having previously produced a report for the Agency meeting these guidelines [*Assessing the impact of heat treatment on antimicrobial resistance genes and their potential uptake by other 'live' bacteria*, FS307036.]). A database of the articles included in the review will also be provided. The database will be in a format suitable for publication on the FSA website. The technical report will identify the impact of biocides and/or heavy metals used in food animal production on the development of AMR. The report will also highlight any information gaps and identify and recommend areas for further work.

The report will include a lay summary, executive summary, introduction (including the background and aims/objectives of the study), methodology, and key findings of the review, discussions, conclusions, what remains unknown, uncertainty around findings, and recommendations for further work. The criteria for selection and non-selection of articles relevant for consideration in the review will also be clearly identified in the report.

Task 4.1: Write up draft final report (Month 6)

A draft final report will be submitted at least 4 weeks before the final report is due to allow time for Agency officials to provide comments.

Task 4.2: Write up final report (Month 7 to 8)

Following consultation with the Agency after completion of the draft final report, a final report will be produced.

Deliverables:

M4: Project completed (Objective 4 complete)

D4: Draft of the final report (Task 4.1 complete)

D5: Final report (Task 4.2 complete), including database of articles included in the review

Objective 5: Dissemination – dissemination of the findings of the project on the evidence on the impact of biocides and/or heavy metals used in food animal production on the development of AMR

Timescale: Month 8 and beyond

Staff: All of the project team.

A full dissemination and exploitation plan will be agreed with the FSA Project Officer during the project. A meeting will be held with FSA officials after completion of the final report to discuss the key project findings and recommendations arising from the review (Task 5.1).

In addition to the final report the findings of the project will be disseminated to key stakeholders in the form of a scientific paper (with the approval of the funder) and presentations. Example dissemination activities may include:

1. An executive summary document / press release agreed with the Agency and distributed to key stakeholders.

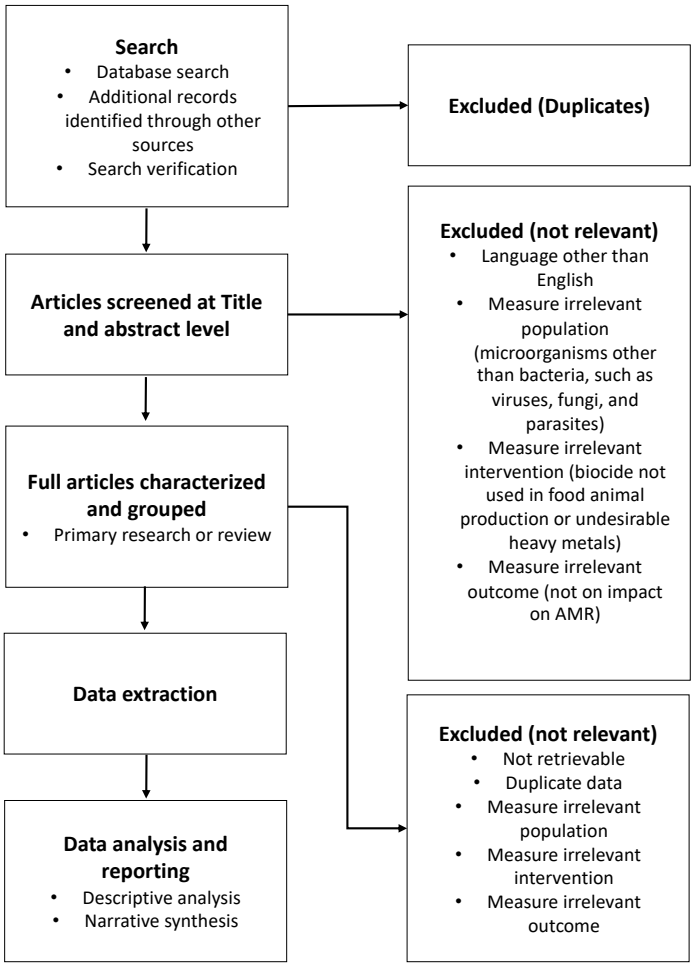
2. At least one key paper will be submitted on “A comprehensive critical review of the impact of impact of biocides and/or heavy metals used in food animal production on the development of AMR” for consideration for publication in a suitable peer-reviewed open access journal.
3. The presentation of results at any FSA conference, workshop, seminar, or related event, as required.
4. Presenting, or supporting the presentation, of the findings of this work at a future FSA AMR ‘show and tell’ event, ACMSF (or AMR sub-group) meetings, and at stakeholder meetings, if needed.
5. Assisting the FSA in producing documents involved in the publication of the study findings which will include a Q&A document and providing comments on news story.
6. Presentation of the study at the FSA’s AMR R&E Programme Review on 8th and 9th November 2022.
7. Presentation of key findings from the study to be given to the ACMSF working group on AMR in early 2023 (FSA to confirm date in due course but likely to be in either January or February 2023).

Deliverables:

D6: Presentation of key findings from the study to be given to the ACMSF working group on AMR by February 2023.

See Gantt and Deliverables table for further information.

A flow chart of the knowledge synthesis process for this review is shown below:



The Gantt chart below sets out the work timetable for this proposed project:

	Project Year / Month							
	2022						2023	
	Mid July	Aug	Sept	Oct	Nov	Dec	Jan	Feb
Objectives, Tasks, Milestones, and Deliverables	1	2	3	4	5	6	7	8
Objective 1: Literature search								
Task 1.1: Agreement of review question, keywords, scope, and eligibility criteria								
Task 1.2: Literature search								
Task 1.3: Collation of articles								
Task 1.4: Revisit								
Objective 2: Article screening								
Task 2.1: Selection of articles for data extraction								
Mid-point interim review								
Objective 3: Data extraction and analysis								
Task 3.1: Data extraction from relevant articles and analysis								
Objective 4: Data synthesis and report completion								
Task 4.1: Write up draft final report								
Task 4.2: Write up final report								
Objective 5: Dissemination								
Task 5.1: Presentation of findings to ACMSF working group on AMR								
Milestones	M1		M2		M3			M4
Deliverables			D1,D2	D3		D4		D5,D6

B. Deliverables

Please outline the proposed project milestones and deliverables. Please provide a timetable of key dates or significant events for the project (for example fieldwork dates, dates for provision of research materials, draft and final reporting). Deliverables must be linked to the objectives.
For larger or more complex projects please insert as many deliverables /milestones as required.
Each deliverable should be:

i. no more 100 characters in length
ii. self-explanatory
iii. cross referenced with objective numbers i.e. deliverables for Objective 1 01/01, 01/02 Objective 2 02/01, 02/02 etc

Please insert additional rows to the table below as required.

A final deliverable pertaining to a retention fee of 20% of the total value of the prosed work will automatically be calculated on the financial template.

Deliverable number or	Target D	TITLE of Deliverable or milestone
M1	**18/07/2022**	**Project start / First project meeting (Task 1.1)**
D1 (1/1)	**01/09/2022**	**Submit database of initial results of literature search completed to the FSA (Task 1.3)**
D2 (2/1)	**27/09/2022**	**Submit completed screened database of relevant collated citations and abstracts to the**

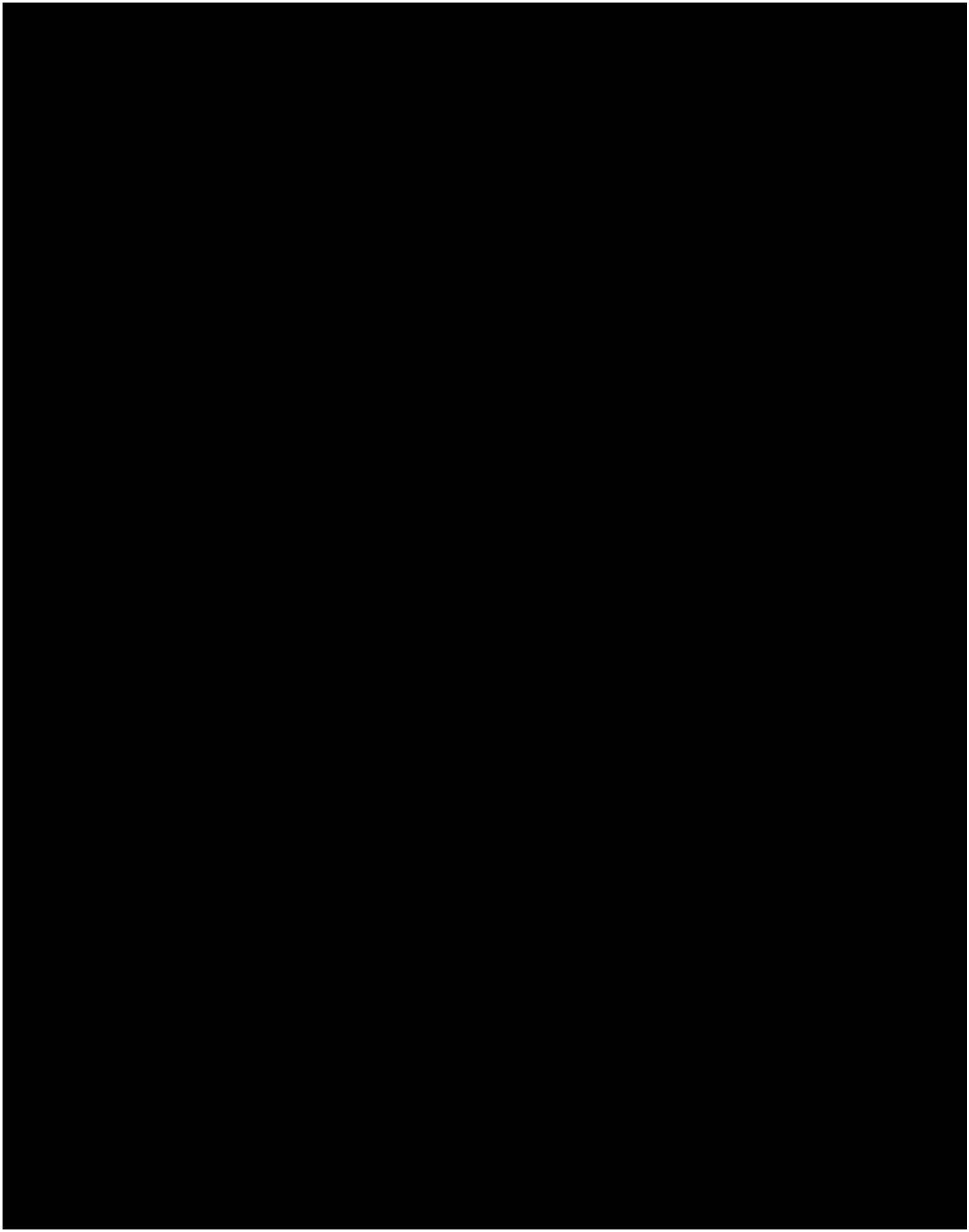
		FSA (Task 2.1)
M2	30/09/2020	Initial literature search and screening completed (Objectives 1 and 2 complete)
D3	27/10/2022	Submit mid-point interim project progress report to the FSA (progress on Objectives 1, 2, and 3)
M3	30/11/2022	Data extraction and analysis of individual articles completed (Objective 3 complete)
D4 (4/1)	19/12/2022	Submit draft of the final report to the FSA (Task 4.1)
D5 (4/2)	20/02/2023	Submit final report to the FSA (Task 4.2)
M4	28/02/2023	Project completed (All objectives and tasks complete)
D6 (5/1)	28/02/2023	Presentation of key findings from the study to the ACMSF working group on AMR (Task 5.1)

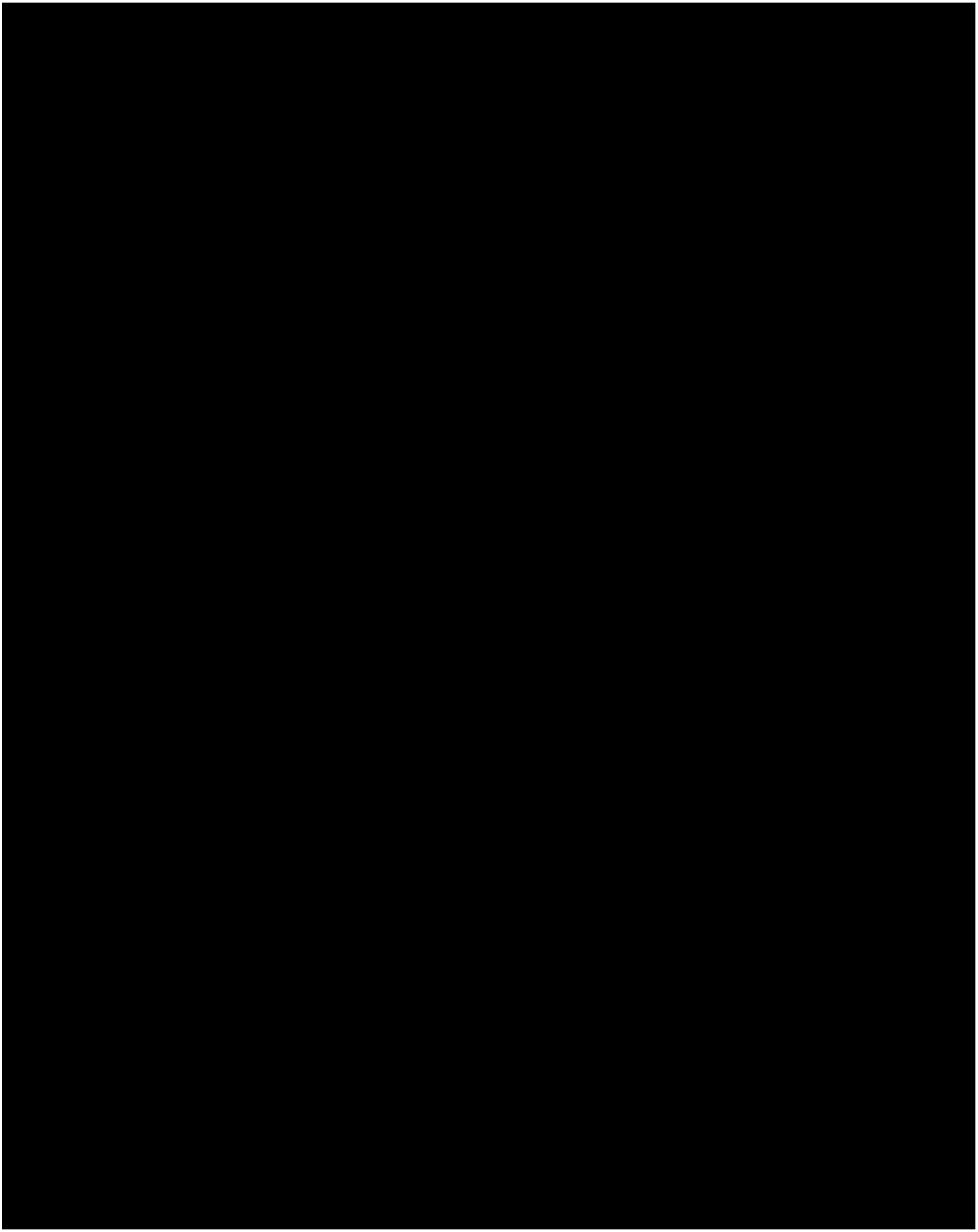
4: ORGANISATIONAL EXPERIENCE, EXPERTISE and STAFF EFFORT

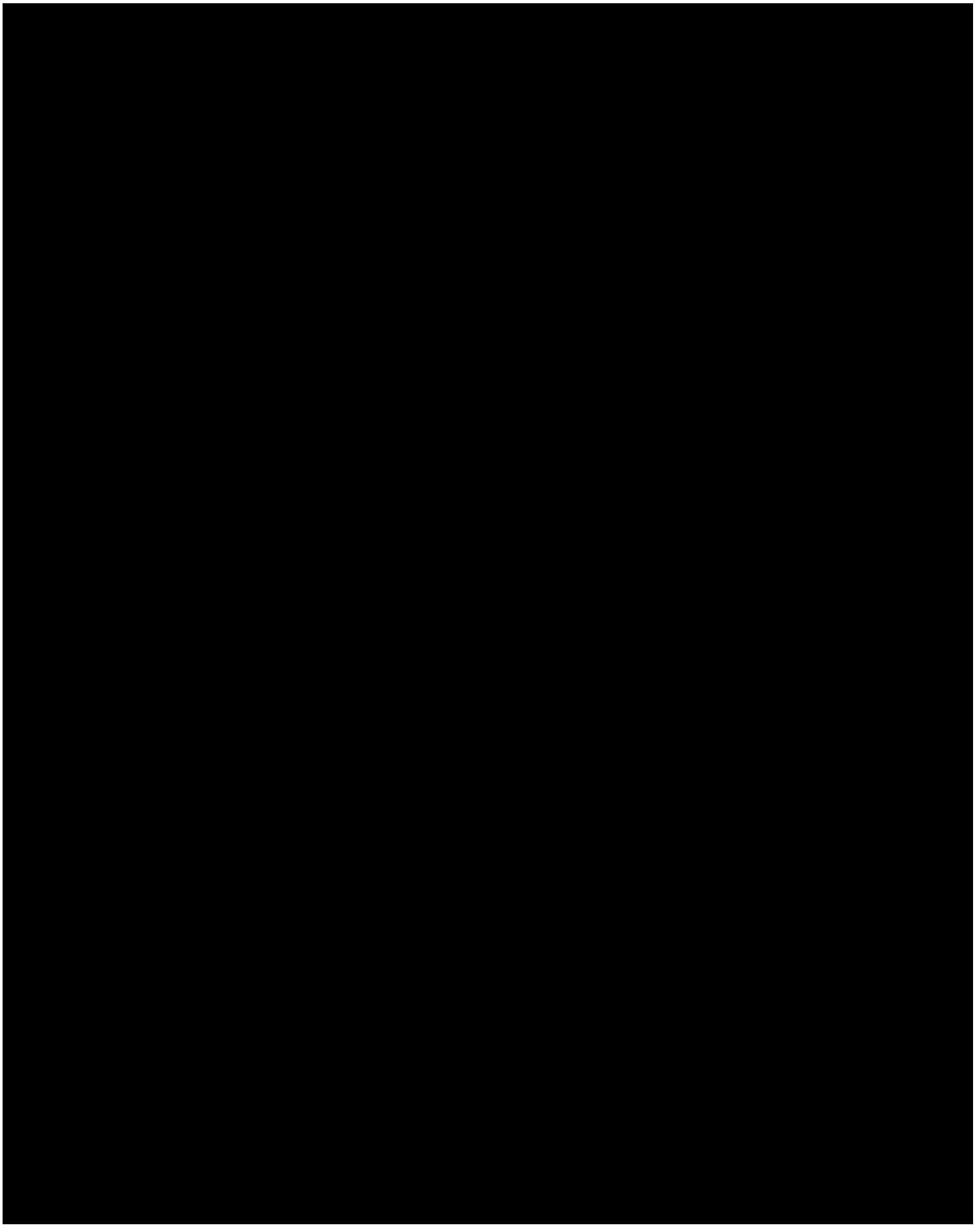
A. PARTICIPATING ORGANISATIONS' PAST PERFORMANCE

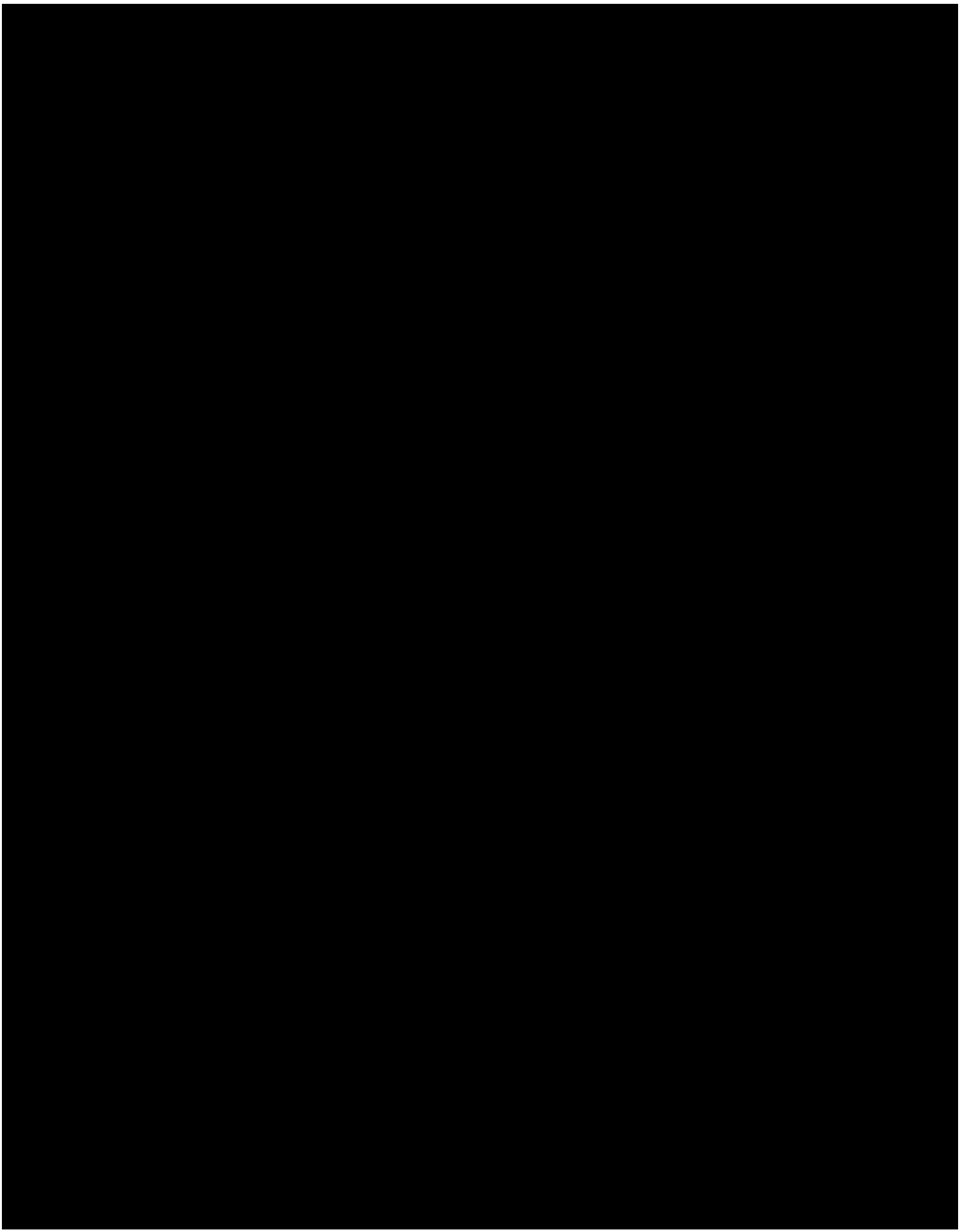
Please provide evidence of up to three similar projects that the project lead applicant and/or members of the project team are currently undertaking or have recently completed. Please include:

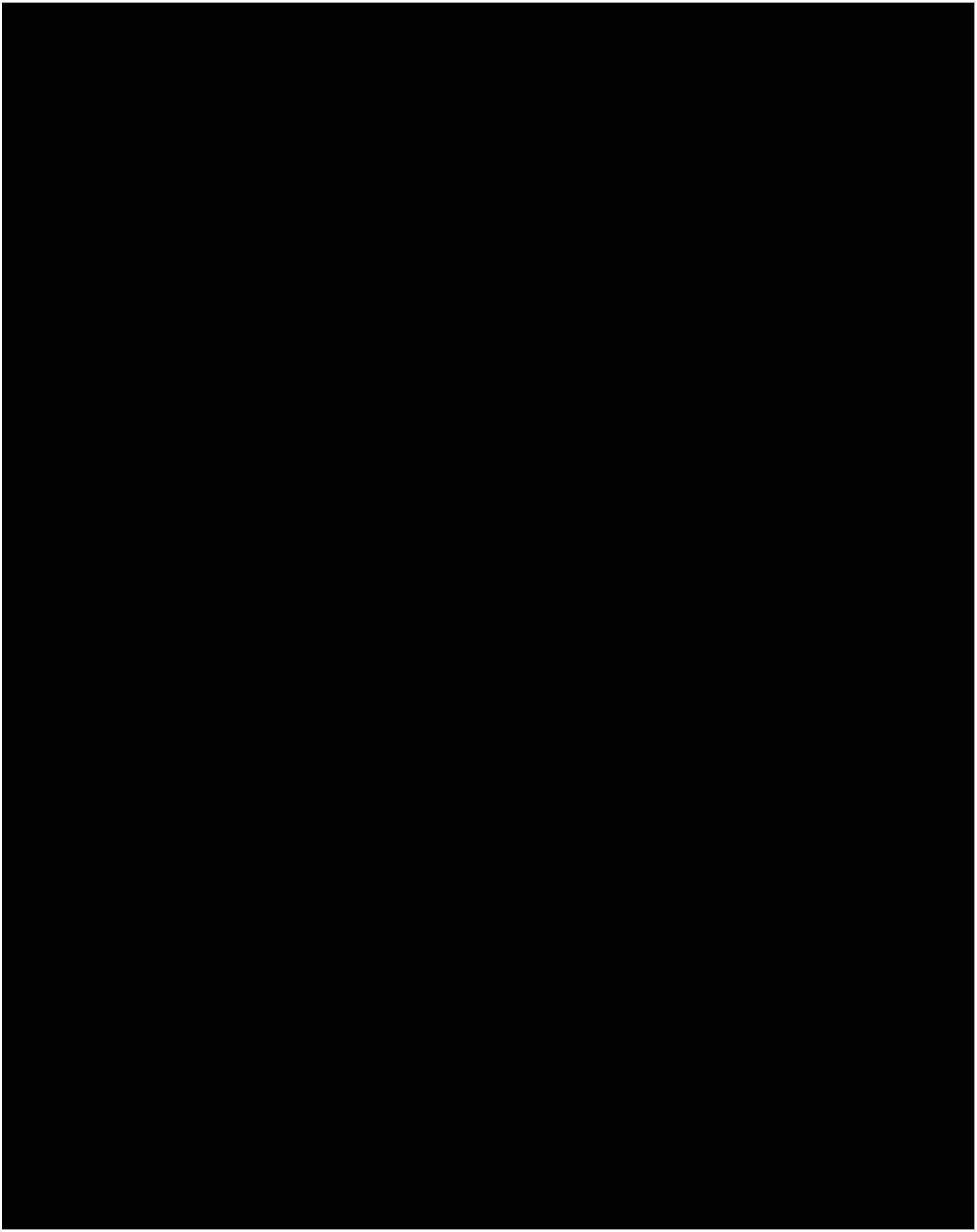
- The start date (and if applicable) the end date of the project/(s)
- Name of the client who commissioned the project?
- Details of any collaborative partners and their contribution.
- The value.
- A brief description of the work carried out.
- How the example(s) demonstrate the relevant skills and/or expertise.
- What skills the team used to ensure the project (s) were successfully delivered.











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[redacted]

C. STAFF EFFORT

In the table below, please detail the staff time to be spent on the project (for every person named in section above) and their role in delivering the proposal If new staff will be hired in order to deliver the project please include their grade, name and the staff effort required.

[redacted]

5: PROJECT MANAGEMENT

Please fully describe how the project will be managed to ensure that objectives and deliverables will be achieved on time and on budget. Please describe how different organisations/staff will interact to deliver the desired outcomes.
Highlight any in-house or external accreditation for the project management system and how this relates to this project.

The project team responsible for designing and delivering the project are experienced and qualified in managing and implementing research, including running large and small multi-discipline, multi-partner Agency, DEFRA, Innovate UK, and EU projects.

The project team will consist of the following members: [redacted] The PI will arrange monthly informal teleconference meetings with the project team to discuss progress, possible risks and ensure that the project is on target to deliver all of the objectives; at critical times (e.g., the start of the project) these may happen more frequently. More formal project review meetings, starting with the kick-off meeting will also be held with the team and the Agency Project Officer. In these meetings project progress and results will be formally reviewed and discussed. The meetings will provide a good opportunity for scientific discussions and making key decisions for the project.

The project will also be subject to senior management scrutiny at the Grimsby Institute via regular project monitoring meetings that take place monthly to review project's progress and finances. Internally, at the Grimsby Institute, this project will be managed and controlled using Prince 2 principles. An internal Project Management Team will be established at the start of the project, comprising the three members of the FRPERC project team, plus the Executive Director of Projects and Partnerships ([redacted] who will maintain oversight for the successful delivery of this project. His role will be to oversee the work programme and verify that all deliverables are on time and to the standard required. The team will meet on a regular basis (minimum monthly) to monitor and review budget, risk register, and performance against the delivery plan. In the event that the project diverts from the delivery plan, SMART targets will be designed, and recovery plans put in place, these will be monitored by the Executive Director for Projects and Partnerships. Project performance will be reported to the Institute's Senior Management Team and Corporation via the Executive Director, providing assurance that project activities will be scrutinised at the highest level.

Regarding Risk Management, all relevant risks in delivering this project on time and to budget and how they will be managed by the project team are detailed in Section 6. The PI will create a risk register at the start of the project, which will be reviewed on a monthly basis, with the project team and at internal project monitoring meetings, to monitor the identified risks, to ensure any new risks which may impede the progress of the project are added to the register, and to ensure contingency plans are in place for such events. The project team meetings will primarily be monitoring and reviewing technical risks, while the internal project monitoring meetings will be monitoring and reviewing risks in delivering the project on time and to budget.

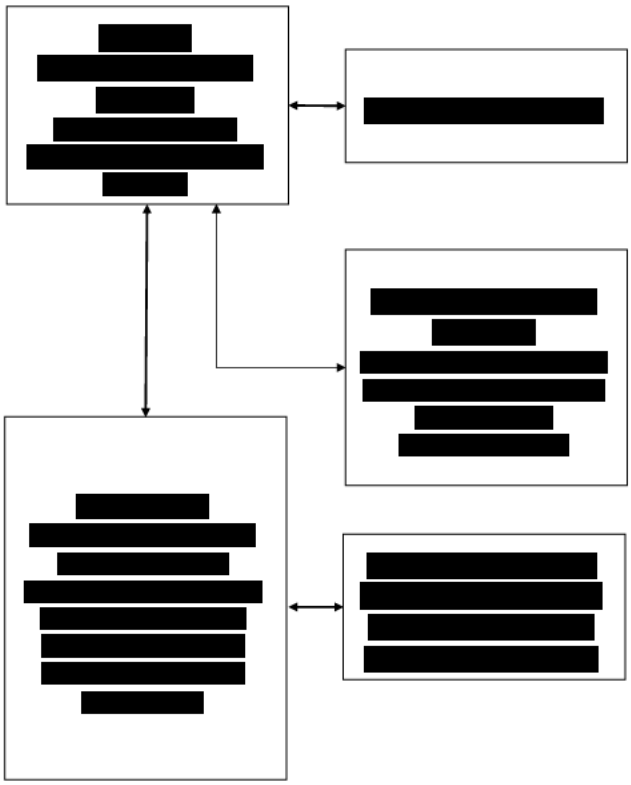
The FSA project manager will receive a monthly update on or around the 26th of each month from principal investigator, [redacted] This should consist of a few lines on whether the project is running to schedule and any risk/issues which could potentially impact the delivery of the project. This information is used as evidence by the FSA project manager to fulfil their own monthly project finance reporting to the FSA's finance department and to track that the project is running according to schedule and the funds will be released as expected.

Key personnel and their roles within this project are as follows:

[redacted]

reviewing of the literature and final report writing stages.

[redacted]



6. RISK MANAGEMENT

In the table provided, please identify all relevant risks in delivering this project on time and to budget. Briefly outline what steps will be taken to minimise these risks and how they will be managed by the project team.
Please add more lines as required

Identified risk	Likelihood of risk (high, medium, low)	Impact of Risk (high, medium, low)	Risk management strategy
Achieving Timeframe	Medium	Medium	Based upon significant past experience of similar projects, we have carefully considered the scope of the data collection and assessments required, and the time required to carry them out. Contingency has been built into the project plan for each Objective for delays in accessing or collating data. We have considered past challenges that have led to time overruns, and built in a sensible catch-up phase for each objective. A full delivery plan and risk register will be implemented and maintained for this project, which will be overseen by an experienced project manager

			at Executive Director level. The project team will meet monthly to review progress to date. This will ensure that any variations from the delivery plan are identified, and remedial action is approved and directed in a timely manner.
Insufficient data available	Low	High	Lack of published data in the topic area of the impact of biocides and/or heavy metals on AMR in food animal production is beyond the control of the consortium. However, the well-structured and broad reaching paper search and evaluations processes detailed above will ensure that any relevant articles are collected. In the unlikely event that there is truly a dearth of basic information then by agreement with Agency at the mid-term review the project workplans will be modified to how best to address the gaps.
Too much data available	Medium	High	A preliminary search of articles has been conducted and suggests that this is a low risk. If excessive numbers of articles are revealed, a second pass with more specific keyword will be made to reduce to a manageable number of articles.
Data access challenges	Low	High	The Participant Organisations have access to the databases required for this work and access to the key academic journals that are likely to have relevant articles. Loss of access to article abstracting services would have a major impact but this is highly unlikely as it is a central research tool used by the Participant Organisations. Contingency has been made in the budget for obtaining any paying for any additional access to articles / chapters / books / reports.
Data quality	Medium	High	In our previous Agency projects, carried out in the past 18 years, we have gathered extensive expertise in assessing and quantifying the quality of the data received. The data evaluation and screening procedures prescribed in the body of the work plan above will apply a weighting to reflect and accommodate the quality of data in each reviewed source.
Budget overruns	Low	Low	The budget has been compiled by an experienced team, who have carried out many projects of this nature over the past decades without overruns. We do not consider it a risk in this project. However, regular monitoring and tracking of expenditure will ensure potential budget over / underspend is identified and addressed at an early stage. This is a fixed price contract, so any budget overrun will be absorbed by the proposers, which mitigates all financial risk to the Agency.
A member of the project team falls ill or leaves	Low	Medium	The main Participant Organisations comprise a pool of experienced staff with relevant experience, sufficient to cover for sickness / if a staff member leaves. Whilst all project team members bring specific expertise to the work, the loss of one individual could be covered by the remaining members of the team. A team approach with several staff capable of covering most areas will significantly reduce impact if one person is unexpectedly

			unavailable for a short period of time.
Recruitment	Low	Low	Failure to recruit the required qualified staff is not a risk in this work, as the key specified staff are currently available to work on the proposed project. All the team will be in place and are available to work on this project from the 1st August 2022 onwards.
IP	Low	Low	The aim of the project is to review publicly available information. There are no expected IP issues.
Infrastructure: Loss of research facilities/resources due to emergency e.g. fire	Low	Low	Since the review will be desk-based work it should not be affected by any loss of specific host research facilities/resources. Back-up systems are in place and loss of access due to an IT network failures etc would only be temporary and not have a major impact in a 6 month project.
Disruption caused by COVID-19	Low	Low	We do not consider COVID-19 to be significant risk to this project. A similar review was carried out by the applicants while COVID-19 restrictions were in place without any significant impact on that similar project. If restrictions are in place, they shouldn't impact on the project progress too much as the project is desk based and the staff are used to working from home and distance working. Regular teleconferences will be used to maintain team working and cohesion.
Other Risks			The PI will create a risk register at the start of the project, which will be reviewed on a monthly basis to monitor identified risks, to ensure any new risks which may impede the progress of the project are added to the register, and to ensure contingency plans are in place for such events.

7. Quality Management

A. QUALITY MANAGEMENT

Please provide details of the measures that will be taken to manage and assure the quality of work. You should upload your Quality Assurance policy in the supporting documents section of your application.

This should include information on the quality assurance (QA) systems, , which have been implemented or are planned, and should be appropriate to the work concerned. All QA systems and procedures should be clear and auditable, and may include compliance with internationally accepted quality standards specified in the ITT e.g. ISO 9001 and ISO17025.

Specific to science projects and where relevant, applicants must indicate whether they would comply with the Joint Code of Practice for Research (JCoPR). If applicants do not already fully comply with the JCoPR please provide a statement to this effect to provide an explanation of how these requirements will be met. The FSA reserves the right to audit projects against the code and other quality standards

The lead principle investigator is responsible for all work carried out in the project; (including work supplied by sub-contractors) and should therefore ensure that the project is carried out in accordance with the Joint Code of Practice

All members of the team and the organisations that they work for aware of the requirements of the Joint Code of Practice for Research (JCoPR) and are committed to conducting research projects in accordance with good scientific practice. Having had wide experience of research projects all of the research teams and individuals involved in this project are aware of the need to ensure that all work is quality assured. This will be achieved through ensuring that Project goals and process are achieved in line with the proposed timeline; regular project progress reporting; regular supervision in relation to the Project with the supervisory team; feedback from participants within the Project. This project has been

designed to comply with the joint code of practice for research.

Regarding the specific requirements of the Code, the lead PI shall endeavour to ensure that the project is carried out in accordance with the Code in the following ways:

QUALITY ISSUE	EVIDENCE
1. Responsibilities	An organisational structure showing line management responsibilities (organogram) for this project are shown in the tender application. We will consistently maintain and update a list of personnel involved with the project. We will have in place a documented agreement with our sub-contractor to adhere to JCoPR and evidence of rationale for appointment. We will maintain files documenting the roles & responsibilities for all project staff (including subcontractors) throughout the project.
2. Personnel competence	Brief CV's of all personnel associated with the project (including subcontractors) are contained within the tender application. Full CV's will be documented at the start of the project. We will maintain relevant, up-to-date training records for all project staff (including evidence showing awareness of obligation to comply with the Code's provisions).
3. Project planning	Since this is a desk-based project specific risk assessments are not required. Records will be maintained of the regular quarterly research project meetings that will include reviews of project timetables and plans. A proposed project plan with milestones and deliverables is contained in the proposal. This will be reviewed monthly by the research project team. Any changes will be formally agreed with the Agency. We suggest that the uncertainty in this review will be investigated in a qualitative manner following the procedure detailed in the EFSA guidance on uncertainty analysis in scientific assessments (EFSA Scientific Committee, 2018a,b). Any method will be agreed between the research project team and Agency. Documented, approved procedures for sampling materials is not required for this particular project. Ethical approval documentation and project licenses are not required for this particular project.
4. Quality Control	The main Participant Organisations operate documented internal 'fit for purpose' review procedures The main Participant Organisations maintain records of consistently applied internal audits and any relevant findings and corrective actions to be taken will documented at quarterly project review meetings. The main Participant Organisations maintain an approved publication policy with authorisation procedures.
5. Health & safety	No specific documentation will be required for this particular desk-based project.
6. Handling of samples & materials	Not applicable to this particular desk-based project.
7. Facilities & equipment	A desk-based project of this nature only requires suitable computing, internet access, database access, and data storage facilities, which the main Participant Organisations have. Collected data will be stored on secure independent back-up systems.

8. Documentation of procedures & methods	We maintain a robust process for document and version control in all key project documentation. The Participant Organisations and research teams have carried out a number of similar literature survey projects of this nature and have therefore developed standard operating procedures for carrying out such work.
9.Research/work records	In this project the majority of the data will be collected and stored electronically, and the small amount of paper documentation collected will be scanned and held electronically. All raw data, searches and reports will be stored in a consistent file structure on a range of independent back-up systems. All data will be securely stored and regularly backed-up to secure systems. The main Participant Organisations have consistent and documented archiving procedures.
10. Field-based research	Not applicable to this particular project.

[redacted]

FRPERC is part of the Grimsby institute (which in turn is part of the TEC Partnership) which has an institute-wide quality assurance policy covering externally funded research projects. FRPERC adheres to these policies and operates a fully documented task orientated job management structure. A fully audited set of records is produced for all studies or parts of studies undertaken by FRPERC. All research undertaken by FRPERC is subject to randomly selected internal audit and the research undertaken by the organisation as a whole is assessed by periodic external academic peer review. Standard operating procedures, protocols and risk assessments are prepared for all work. In addition, the Grimsby Institute conduct research for companies on a regular basis as well as for other publicity funded research bodies.
Researchers at the Universities of Lincoln and Liverpool both operate within their Universities Code of Research Practice. They both conduct regular internal audits of projects.

B. DATA PROTECTION

Please identify any specific data protection issues for this project and how these will be managed. Please respond to any specific issues raised in the Specification document.
Please note that the successful Applicant will be expected to comply with the Data Protection Act (DPA) 1998 and ensure that any information collected, processed and transferred on behalf of the FSA, will be held and transferred securely.

In this part please provide details of the practices and systems which are in place for handling data securely including transmission between the field and head office and then to the FSA. Plans for how data will be deposited (i.e. within a community or institutional database/archive) and/or procedures for the destruction of physical and system data should also be included in this part (this is particularly relevant for survey data and personal data collected from clinical research trials). The project Lead Applicant will be responsible for ensuring that they and any sub-contractor who processes or handles information on behalf of the FSA are conducted securely.

We do not envisage any specific data protection issues with this project. Of course, any commercially sensitive information obtained from any participating stakeholders will remain confidential. The team will process any personal data provided to them in accordance with the EU General Data Protection Regulation (GDPR), which came in to force on the 25th of May 2018, and any associated or subsequent legislation, Code of Practice or Statutory Instrument. The institutions to which the project team are members have established Data Protection Policies and procedures in accordance with current legislation. This policy applies to all staff, including temporary, casual or agency staff and contractors, consultants, research students, and suppliers working for, or on behalf of, either institution. They will take reasonable precautions to keep such personal data secure and to prevent unauthorised disclosure. Good research practice standards will be applied for the collection, management, and storage of all data collected.

C. DISSEMINATION AND EXPLOITATION

Where applicable please indicate how you intend to disseminate the results of this project, including written and verbal communication routes if appropriate. Applicants are advised to think carefully about how their research aligns with the FSA strategy, what is the impact that their research has on public health/ consumers and decide how the results can best be communicated to the relevant and appropriate people and organisations in as cost-effective manner as possible. Please provide as much detail as possible on what will be delivered. Any costs associated with this must be documented in the Financial Template.

The applicant should describe plans for the dissemination of the results for the project team as a whole and for individual participants. Details should include anticipated numbers of publications in refereed journals, articles in trade journals etc., presentations or demonstrations to the scientific community, trade organisations and internal reports or publications. Plans to make any information and/or reports available on the internet with the FSA's permission are also useful, however, this does not remove the requirement for Tenderers to think how best to target the output to relevant groups.
If a final report is part of the requirement, please make sure, as part of the executive summary, that aims and results are clear to the general audience and that the impact of the research on public health/consumers and it's alignment to FSA priorities is clearly stated.

Please note that permission to publish or to present findings from work supported by the FSA must be sought in advance from the relevant FSA Project Officer. The financial support of the FSA must also be acknowledged.

Please indicate whether any Intellectual Property (IP) may be generated by this project and how this could be exploited. Please be aware the FSA retains all rights to the intellectual property generated by any contract and where appropriate may exploit the IP generated for the benefit of public health.
In this part Applicants should demonstrate the credibility of the partnership for exploitation of the results and explain the partnership's policy in respect of securing patents or granting licenses for the technology (if applicable). It should deal with any possible agreements between the partners to extend their co-operation in the exploitation phase and with relevant agreements with companies, in particular users, external to the partnership

We are aware of the Agency's commitment to openness and transparency. The expected output of this project will be a critical review of the scientific literature on the AMR hazards and risks arising as a consequence of biocide and/or heavy metal use in food animal production, and a database of the articles included in the review, both suitable for publication on the FSA website. Following submission of the final report, the project team will discuss the key findings and recommendations arising from the research with the Agency. We also understand that the findings may also be required to be presented to ACMSF at a future meeting and will be happy to do so. As well as the final project report being published by the Agency, we will agree with the Agency on appropriate methods to further disseminate the findings of this research to a wider audience. A full dissemination and exploitation plan will be agreed with the FSA Project Officer during the project. Example dissemination activities may include:

- An executive summary document / press release agreed with the Agency and distributed to key stakeholders.
- Placement of project summaries on the websites of FRPERC (TEC Partnership) and the University of Lincoln which carry articles concerning R&D projects and a source of useful reference data for industry.
- The ultimate findings are expected to be of scientific merit and at least one key paper will be submitted on "A comprehensive critical review of the impact of impact of biocides and/or heavy metals used in food animal production on the development of AMR" for consideration for publication in a suitable peer-reviewed open access journal, such as *Antibiotics*.
- The presentation of results at any FSA conference, workshop, seminar, or related event, as required.
- Giving a presentation on this study at the FSA's AMR R&E programme review event to be held on 8th and 9th November 2022.
- Present key findings from this study to the ACMSF working group on AMR in early 2023 (either January or February).
- Assisting the FSA in producing documents involved in the publication of the study findings which will include a Q&A document and providing comments on any news story.

The findings of this research will be disseminated bearing these points in mind:

- The findings from throughout this project will be finalised and made public only after agreement of the FSA Project Officer has been obtained.
- Any presentation of findings will include full acknowledgement of the funder (FSA) as providing financial support.

The aim of the project is to review publicly available information. It is not expected that any Intellectual Property (IP) will be generated by this project.

Annex 4 - Charges

Tender Reference	FS430957

Tender Title	Critical review of AMR risks arising as a consequence of using biocides and certain heavy metals in food animal production

Full legal organisation name	TEC Partnership

Main contact title	[redacted]
Main contact forname	[redacted]
Main contact surname	[redacted]

Main contact position	[redacted]
Main contact email	[redacted]
Main contact phone	[redacted]

Will you charge the Agency VAT on this proposal?	No

Please state your VAT registration number:	

Project Costs Summary Breakdown by Participating Organisations
Please include only the cost to the FSA.

Organisation	VAT Code *	Total (£)
[redacted]		
		£ -

		£ -
		£ -

Total Project Costs (excluding VAT) **	**£ 36,941.12**

* Please indicate zero, exempt or standard rate. VAT charges not identified above will not be paid by the FSA
** The total cost figure should be the same as the total cost shown in table 4
** The total cost figure should be the same as the total cost shown below and in the Schedule of payments tab.

Project Costs Summary (*Automatically calculated*)

Total Project Costs	**£ 36,941.12**

COST OR VOLUME DISCOUNTS - INNOVATION

The Food Standards Agency collaborates with our suppliers to improve efficiency and performance to save the taxpayer money. A tenderer should include in his tender the extent of any discounts or rebates offered against their normal day rates or other costs during each year of the contract. Please provide full details below:
[redacted]

SIGNATURE	[redacted]	
NAME		
DATE	16-May-2022	
REVISION DATE	11-Jul-2022	Enter the effective date if this version of the template replaces an earlier version

Staff Costs Table

*This should reflect details entered in your technical application section 4C.

Please insert as many lines as necessary for the individuals in the project team.

Please note that FSA is willing to accept pay rates based upon average pay costs. You will need to indicate where these have been used.

* Role or Position within the project	Participating Organisation	Daily Rate (£/Day)	* Daily Overhead Rate(£/Day)	Days to be spent on the project by all staff at this grade	**Total Cost (incl. overheads)**
[redacted]					

Consumable/Equipment Costs

Please provide a breakdown of the consumables/equipment items you expect to consume during the project

Please provide, in the table below, estimates of other costs that do not fit within any other cost headings

The Pricing Schedule

Please complete a proposed schedule of payments below, **excluding VAT** to be charged by any subcontractors to the project lead
applicant. This must add up to the same value as detailed in the Summary of project costs to FSA including participating

organisations costs.

Where differing rates of VAT apply against the deliverables please provide details on separate lines.
Please link all deliverables (singly or grouped) to each payment. Please ensure that deliverable numbers are given as well as a
brief description e.g. Deliverable 01/02: interim report submitted to the FSA, monthly report, interim report, final report
Payment will be made to the Contractor, as per the schedule of payments upon satisfactory completion of the deliverables.

Proposed Project Start Date	**18-Jul-2022**	**Amount**				
Invoice Due Date	**Description as to which deliverables this invoice will refer to (*Please include the deliverable ref no(s) as appropriate*)**	***Net**	****** VAT Code**	**§ Duration from start of project (Weeks)**	**§ Duration from start of project (Date)**	**Financial Year**
[redacted]						

[redacted]

Total	**£ 36,941.12**

* Please insert the amount to be invoiced net of any VAT for each deliverable
** Please insert the applicable rate of VAT for each deliverable
*** 20% of the total project budget is withheld and will be paid upon acceptance of a satisfactory final report by the agency.
§The number of weeks after project commencement for the deliverable to be completed

Summary of Payments

	Year 1		
Financial Year (Update as applicable in YYYY-YY format)	**2022-23**	Retention	Total
Total Amount	[redacted]	[redacted]	**£ 36,941.12**

Short form Terms

1. Definitions used in the Contract

In this Contract, unless the context otherwise requires, the following words shall have the following meanings:

"Central Government Body"	means a body listed in one of the following sub-categories of the Central Government classification of the Public Sector Classification Guide, as published and amended from time to time by the Office for National Statistics: a) Government Department; b) Non-Departmental Public Body or Assembly Sponsored Public Body (advisory, executive, or tribunal); c) Non-Ministerial Department; or d) Executive Agency;
"Charges"	means the charges for the Deliverables as specified in the Order Form;
"Confidential Information"	means all information, whether written or oral (however recorded), provided by the disclosing Party to the receiving Party and which (i) is known by the receiving Party to be confidential; (ii) is marked as or stated to be confidential; or (iii) ought reasonably to be considered by the receiving Party to be confidential;
"Contract"	means the contract between (i) the Buyer and (ii) the Supplier which is created by the Supplier's counter signing the Order Form and includes the Order Form and Annexes;
"Controller"	has the meaning given to it in the GDPR;
"Buyer"	means the person identified in the letterhead of the Order Form;
"Date of Delivery"	means that date by which the Deliverables must be delivered to the Buyer, as specified in the Order Form;
"Buyer Cause"	any breach of the obligations of the Buyer or any other default, act, omission, negligence or statement of the Buyer, of its employees, servants, agents in connection with or in relation to the subject-matter of the Contract and in respect of which the Buyer is liable to the Supplier;
"Data Protection Legislation"	(i) the GDPR, the LED and any applicable national implementing Laws as amended from time to time (ii) the Data Protection Act 2018 to the extent that it relates to processing

	of personal data and privacy; (iii) all applicable Law about the processing of personal data and privacy;
"Data Protection Impact Assessment"	an assessment by the Controller of the impact of the envisaged processing on the protection of Personal Data;
"Data Protection Officer"	has the meaning given to it in the GDPR;
"Data Subject"	has the meaning given to it in the GDPR;
"Data Loss Event"	any event that results, or may result, in unauthorised access to Personal Data held by the Supplier under this Contract, and/or actual or potential loss and/or destruction of Personal Data in breach of this Contract, including any Personal Data Breach;
"Data Subject Access Request"	a request made by, or on behalf of, a Data Subject in accordance with rights granted pursuant to the Data Protection Legislation to access their Personal Data;
"Deliver"	means hand over the Deliverables to the Buyer at the address and on the date specified in the Order Form, which shall include unloading and any other specific arrangements agreed in accordance with Clause [ ]. Delivered and Delivery shall be construed accordingly;
"Existing IPR"	any and all intellectual property rights that are owned by or licensed to either Party and which have been developed independently of the Contract (whether prior to the date of the Contract or otherwise);
"Expiry Date"	means the date for expiry of the Contract as set out in the Order Form;
"FOIA"	means the Freedom of Information Act 2000 together with any guidance and/or codes of practice issued by the Information Commissioner or relevant Government department in relation to such legislation;
"Force Majeure Event"	any event, occurrence, circumstance, matter or cause affecting the performance by either Party of its obligations under the Contract arising from acts, events, omissions, happenings or non-happenings beyond its reasonable control which prevent or materially delay it from performing its obligations under the Contract but excluding: i) any industrial dispute relating to the Supplier, the Supplier Staff (including any subsets of them) or any other failure in the Supplier or the Subcontractor's supply chain; ii) any event, occurrence, circumstance, matter or cause which is attributable to the wilful act, neglect or failure to take reasonable precautions against it by the Party concerned; and iii) any failure of delay caused by a lack of funds;

"GDPR"	the General Data Protection Regulation (Regulation (EU) 2016/679);
"Goods"	means the goods to be supplied by the Supplier to the Buyer under the Contract;
"Good Industry Practice"	standards, practices, methods and procedures conforming to the law and the exercise of the degree of skill and care, diligence, prudence and foresight which would reasonably and ordinarily be expected from a skilled and experienced person or body engaged within the relevant industry or business sector;
"Government Data"	a) the data, text, drawings, diagrams, images or sounds (together with any database made up of any of these) which are embodied in any electronic, magnetic, optical or tangible media, including any of the Buyer's confidential information, and which: i) are supplied to the Supplier by or on behalf of the Buyer; or ii) the Supplier is required to generate, process, store or transmit pursuant to the Contract; or b) any Personal Data for which the Buyer is the Data Controller;
"Information"	has the meaning given under section 84 of the FOIA;
"Information Commissioner"	the UK's independent authority which deals with ensuring information relating to rights in the public interest and data privacy for individuals is met, whilst promoting openness by public bodies;
"Insolvency Event"	in respect of a person: a) if that person is insolvent; ii) if an order is made or a resolution is passed for the winding up of the person (other than voluntarily for the purpose of solvent amalgamation or reconstruction); iii) if an administrator or administrative receiver is appointed in respect of the whole or any part of the persons assets or business; iv) if the person makes any composition with its creditors or takes or suffers any similar or analogous action to any of the actions detailed in this definition as a result of debt in any jurisdiction;
"Key Personnel"	means any persons specified as such in the Order Form or otherwise notified as such by the Buyer to the Supplier in writing;
"LED"	Law Enforcement Directive (Directive (EU) 2016/680);
"New IPR"	all and intellectual property rights in any materials created or developed by or on behalf of the Supplier pursuant to the Contract but shall not include the Supplier's Existing IPR;
"Order Form"	means the letter from the Buyer to the Supplier printed above these terms and conditions;
"Party"	the Supplier or the Buyer (as appropriate) and "Parties" shall mean both of them;
"Personal Data"	has the meaning given to it in the GDPR;

"Personal Data Breach"	has the meaning given to it in the GDPR;
"Processor"	has the meaning given to it in the GDPR;
"Purchase Order Number"	means the Buyer's unique number relating to the order for Deliverables to be supplied by the Supplier to the Buyer in accordance with the terms of the Contract;
"Regulations"	the Public Contracts Regulations 2015 and/or the Public Contracts (Scotland) Regulations 2015 (as the context requires) as amended from time to time;
"Request for Information"	has the meaning set out in the FOIA or the Environmental Information Regulations 2004 as relevant (where the meaning set out for the term "request" shall apply);
"Services"	means the services to be supplied by the Supplier to the Buyer under the Contract;
"Specification"	means the specification for the Deliverables to be supplied by the Supplier to the Buyer (including as to quantity, description and quality) as specified in the Order Form;
"Staff"	means all directors, officers, employees, agents, consultants and contractors of the Supplier and/or of any sub-contractor of the Supplier engaged in the performance of the Supplier's obligations under the Contract;
"Staff Vetting Procedures"	means vetting procedures that accord with good industry practice or, where applicable, the Buyer's procedures for the vetting of personnel as provided to the Supplier from time to time;
"Subprocessor"	any third Party appointed to process Personal Data on behalf of the Supplier related to the Contract;
"Supplier Staff"	all directors, officers, employees, agents, consultants and contractors of the Supplier and/or of any Subcontractor engaged in the performance of the Supplier's obligations under a Contract;
"Supplier"	means the person named as Supplier in the Order Form;
"Term"	means the period from the start date of the Contract set out in the Order Form to the Expiry Date as such period may be extended in accordance with clause [ ] or terminated in accordance with the terms and conditions of the Contract;
"US-EU Privacy Shield Register"	a list of companies maintained by the United States of America Department for Commence that have self-certified their commitment to adhere to the European legislation relating to the processing of personal data to non-EU countries which is available online at: https://www.privacyshield.gov/list;

"VAT"	means value added tax in accordance with the provisions of the Value Added Tax Act 1994;
"Workers"	any one of the Supplier Staff which the Buyer, in its reasonable opinion, considers is an individual to which Procurement Policy Note 08/15 (Tax Arrangements of Public Appointees) (https://www.gov.uk/government/publications/procurement-policynote-0815-tax-arrangements-of-appointees) applies in respect of the Deliverables;
"Working Day"	means a day (other than a Saturday or Sunday) on which banks are open for business in the City of London.

2. Understanding the Contract

In the Contract, unless the context otherwise requires:

2.1 references to numbered clauses are references to the relevant clause in these terms and conditions;

2.2 any obligation on any Party not to do or omit to do anything shall include an obligation not to allow that thing to be done or omitted to be done;

2.3 the headings in this Contract are for information only and do not affect the interpretation of the Contract;

2.4 references to "writing" include printing, display on a screen and electronic transmission and other modes of representing or reproducing words in a visible form;

2.5 the singular includes the plural and vice versa;

2.6 a reference to any law includes a reference to that law as amended, extended, consolidated or re-enacted from time to time and to any legislation or byelaw made under that law; and

2.7 the word ‘including’, "for example" and similar words shall be understood as if they were immediately followed by the words "without limitation".

3. How the Contract works

3.1 The Order Form is an offer by the Buyer to purchase the Deliverables subject to and in accordance with the terms and conditions of the Contract.

3.2 The Supplier is deemed to accept the offer in the Order Form when the Buyer receives a copy of the Order Form signed by the Supplier.

3.3 The Supplier warrants and represents that its tender and all statements made and documents submitted as part of the procurement of Deliverables are and remain true and accurate.

4. What needs to be delivered

4.1 All Deliverables

(a) The Supplier must provide Deliverables: (i) in accordance with the Specification; (ii) to a professional standard; (iii) using reasonable skill and care; (iv) using Good Industry Practice; (v) using its own policies, processes and internal quality control measures as long as they don't conflict with the Contract; (vi) on the dates agreed; and (vii) that comply with all law.

(b) The Supplier must provide Deliverables with a warranty of at least 90 days (or longer where the Supplier offers a longer warranty period to its Buyers) from Delivery against all obvious defects.

4.2 Goods clauses

(a) All Goods delivered must be new, or as new if recycled, unused and of recent origin.

(b) All manufacturer warranties covering the Goods must be assignable to the Buyer on request and for free.

(c) The Supplier transfers ownership of the Goods on completion of delivery (including off-loading and stacking) or payment for those Goods, whichever is earlier.

(d) Risk in the Goods transfers to the Buyer on delivery, but remains with the Supplier if the Buyer notices damage following delivery and lets the Supplier know within three Working Days of delivery.

(e) The Supplier warrants that it has full and unrestricted ownership of the Goods at the time of transfer of ownership.

(f) The Supplier must deliver the Goods on the date and to the specified location during the Buyer's working hours.

(g) The Supplier must provide sufficient packaging for the Goods to reach the point of delivery safely and undamaged.

(h) All deliveries must have a delivery note attached that specifies the order number, type and quantity of Goods.

(i) The Supplier must provide all tools, information and instructions the Buyer needs to make use of the Goods.

(j) The Supplier will notify the Buyer of any request that Goods are returned to it or the manufacturer after the discovery of safety issues or defects that might endanger health or hinder performance and shall indemnify the Buyer against the costs arising as a result of any such request.

(k) The Buyer can cancel any order or part order of Goods which has not been delivered. If the Buyer gives less than 14 days' notice then it will pay the Supplier's reasonable and proven costs already incurred on the cancelled order as long as the Supplier takes all reasonable steps to minimise these costs.

(l) The Supplier must at its own cost repair, replace, refund or substitute (at the Buyer's option and request) any Goods that the Buyer rejects because they don't conform with clause 4.2. If the Supplier doesn't do this it will pay the Buyer's costs including repair or re-supply by a third party.

(m) The Buyer will not be liable for any actions, claims, costs and expenses incurred by the Supplier or any third party during delivery of the Goods unless and to the extent that it is caused by negligence or other wrongful act of the Buyer or its servant or agent. If the Buyer suffers or incurs any damage or injury (whether fatal or otherwise) occurring in the course of delivery or

installation then the Supplier shall indemnify from any losses, charges costs or expenses which arise as a result of or in connection with such damage or injury where it is attributable to any act or omission of the Supplier or any of its [sub-suppliers].

4.3 Services clauses

(a) Late delivery of the Services will be a default of the Contract.
(b) The Supplier must co-operate with the Buyer and third party suppliers on all aspects connected with the delivery of the Services and ensure that Supplier Staff comply with any reasonable instructions including any security requirements.
(c) The Buyer must provide the Supplier with reasonable access to its premises at reasonable times for the purpose of supplying the Services
(d) The Supplier must at its own risk and expense provide all equipment required to deliver the Services. Any equipment provided by the Buyer to the Supplier for supplying the Services remains the property of the Buyer and is to be returned to the Buyer on expiry or termination of the Contract.
(e) The Supplier must allocate sufficient resources and appropriate expertise to the Contract.
(f) The Supplier must take all reasonable care to ensure performance does not disrupt the Buyer's operations, employees or other contractors.
(g) On completion of the Services, the Supplier is responsible for leaving the Buyer's premises in a clean, safe and tidy condition and making good any damage that it has caused to the Buyer's premises or property, other than fair wear and tear.
(h) The Supplier must ensure all Services, and anything used to deliver the Services, are of good quality [and free from defects].
(i) The Buyer is entitled to withhold payment for partially or undelivered Services, but doing so does not stop it from using its other rights under the Contract.

5. Pricing and payments

5.1 In exchange for the Deliverables, the Supplier shall be entitled to invoice the Buyer for the charges in the Order Form. The Supplier shall raise invoices promptly and in any event within 90 days from when the charges are due.

5.2 All Charges:

(a) exclude VAT, which is payable on provision of a valid VAT invoice;
(b) include all costs connected with the supply of Deliverables.

5.3 The Buyer must pay the Supplier the charges within 30 days of receipt by the Buyer of a valid, undisputed invoice, in cleared funds to the Supplier's account stated in the Order Form.

5.4 A Supplier invoice is only valid if it:

(a) includes all appropriate references including the Purchase Order Number and other details reasonably requested by the Buyer;
(b) includes a detailed breakdown of Deliverables which have been delivered (if any).

5.5 If there is a dispute between the Parties as to the amount invoiced, the Buyer shall pay the undisputed amount. The Supplier shall not suspend the provision of the Deliverables unless the Supplier is entitled to terminate the Contract for a failure to pay undisputed sums in accordance with clause 11.6. Any disputed amounts shall be resolved through the dispute resolution procedure detailed in clause 33.

5.6 The Buyer may retain or set-off payment of any amount owed to it by the Supplier if notice and reasons are provided.

5.7 The Supplier must ensure that all subcontractors are paid, in full, within 30 days of receipt of a valid, undisputed invoice. If this doesn't happen, the Buyer can publish the details of the late payment or non-payment.

6. The Buyer's obligations to the Supplier

6.1 If Supplier fails to comply with the Contract as a result of a Buyer Cause:

(a) the Buyer cannot terminate the Contract under clause 11;
(b) the Supplier is entitled to reasonable and proven additional expenses and to relief from liability under this Contract;
(c) the Supplier is entitled to additional time needed to deliver the Deliverables;
(d) the Supplier cannot suspend the ongoing supply of Deliverables.

6.2 Clause 6.1 only applies if the Supplier:

(a) gives notice to the Buyer within 10 Working Days of becoming aware;
(b) demonstrates that the failure only happened because of the Buyer Cause;
(c) mitigated the impact of the Buyer Cause.

7. Record keeping and reporting

7.1 The Supplier must ensure that suitably qualified representatives attend progress meetings with the Buyer and provide progress reports when specified in the Order Form.

7.2 The Supplier must keep and maintain full and accurate records and accounts on everything to do with the Contract for seven years after the date of expiry or termination of the Contract.

7.3 The Supplier must allow any auditor appointed by the Buyer access to their premises to verify all contract accounts and records of everything to do with the Contract and provide copies for the audit.

7.4 The Supplier must provide information to the auditor and reasonable co-operation at their request.

7.5 If the Supplier is not providing any of the Deliverables, or is unable to provide them, it must immediately:

(a) tell the Buyer and give reasons;
(b) propose corrective action;
(c) provide a deadline for completing the corrective action.

7.6 If the Buyer, acting reasonably, is concerned as to the financial stability of the Supplier such that it may impact on the continued performance of the Contract then the Buyer may:

(a) require that the Supplier provide to the Buyer (for its approval) a plan setting out how the Supplier will ensure continued performance of the Contract and the Supplier will make changes to such plan as reasonably required by the Buyer and once it is agreed then the Supplier shall act in accordance with such plan and report to the Buyer on demand

(b) if the Supplier fails to provide a plan or fails to agree any changes which are requested by the Buyer or fails to implement or provide updates on progress with the plan, terminate the Contract immediately for material breach (or on such date as the Buyer notifies).

8. Supplier staff

8.1 The Supplier Staff involved in the performance of the Contract must:

(a) be appropriately trained and qualified;

(b) be vetted using Good Industry Practice

(c) comply with all conduct requirements when on the Buyer's premises.

8.2 Where a Buyer decides one of the Supplier's Staff isn't suitable to work on the Contract, the Supplier must replace them with a suitably qualified alternative.

8.3 If requested, the Supplier must replace any person whose acts or omissions have caused the Supplier to breach clause 8.

8.4 The Supplier must provide a list of Supplier Staff needing to access the Buyer's premises and say why access is required.

8.5 The Supplier indemnifies the Buyer against all claims brought by any person employed by the Supplier caused by an act or omission of the Supplier or any Supplier Staff.

8.6 The Supplier shall use those persons nominated in the Order Form (if any) to provide the Deliverables and shall not remove or replace any of them unless:

(a) requested to do so by the Buyer (not to be unreasonably withheld or delayed);

(b) the person concerned resigns, retires or dies or is on maternity or long-term sick leave; or

(c) the person's employment or contractual arrangement with the Supplier or any subcontractor is terminated for material breach of contract by the employee.

9. Rights and protection

9.1 The Supplier warrants and represents that:

(a) it has full capacity and authority to enter into and to perform the Contract;

(b) the Contract is executed by its authorised representative;

(c) it is a legally valid and existing organisation incorporated in the place it was formed;

(d) there are no known legal or regulatory actions or investigations before any court, administrative body or arbitration tribunal pending or threatened against it or its affiliates that might affect its ability to perform the Contract;
(e) it maintains all necessary rights, authorisations, licences and consents to perform its obligations under the Contract;
(f) it doesn't have any contractual obligations which are likely to have a material adverse effect on its ability to perform the Contract; and
(g) it is not impacted by an Insolvency Event.

9.2 The warranties and representations in clause 9.1 are repeated each time the Supplier provides Deliverables under the Contract.

9.3 The Supplier indemnifies the Buyer against each of the following:
(a) wilful misconduct of the Supplier, any of its subcontractor and/or Supplier Staff that impacts the Contract;
(b) non-payment by the Supplier of any tax or National Insurance.

9.4 If the Supplier becomes aware of a representation or warranty that becomes untrue or misleading, it must immediately notify the Buyer.

9.5 All third party warranties and indemnities covering the Deliverables must be assigned for the Buyer's benefit by the Supplier.

10. Intellectual Property Rights (IPRs)

10.1 Each Party keeps ownership of its own Existing IPRs. The Supplier gives the Buyer a non-exclusive, perpetual, royalty-free, irrevocable, transferable worldwide licence to use, change and sub-license the Supplier's Existing IPR to enable it and its sub-licensees to both:
(a) receive and use the Deliverables;
(b) use the New IPR.

10.2 Any New IPR created under the Contract is owned by the Buyer. The Buyer gives the Supplier a licence to use any Existing IPRs for the purpose of fulfilling its obligations under the Contract and a perpetual, royalty-free, non-exclusive licence to use any New IPRs.

10.3 Where a Party acquires ownership of intellectual property rights incorrectly under this Contract it must do everything reasonably necessary to complete a transfer assigning them in writing to the other Party on request and at its own cost.

10.4 Neither Party has the right to use the other Party's intellectual property rights, including any use of the other Party's names, logos or trademarks, except as provided in clause 10 or otherwise agreed in writing.

10.5 If any claim is made against the Buyer for actual or alleged infringement of a third party's intellectual property arising out of, or in connection with, the supply or use of the Deliverables (an "**IPR Claim**"), then the Supplier indemnifies the Buyer against all losses, damages, costs or expenses (including professional fees and fines) incurred as a result of the IPR Claim.

10.6 If an IPR Claim is made or anticipated the Supplier must at its own expense and the Buyer's sole option, either:

(a) obtain for the Buyer the rights in clauses 10.1 and 10.2 without infringing any third party intellectual property rights;

(b) replace or modify the relevant item with substitutes that don't infringe intellectual property rights without adversely affecting the functionality or performance of the Deliverables.

11. Ending the contract

11.1 The Contract takes effect on the date of or (if different) the date specified in the Order Form and ends on the earlier of the date of expiry or termination of the Contract or earlier if required by Law.

11.2 The Buyer can extend the Contract where set out in the Order Form in accordance with the terms in the Order Form.

11.3 Ending the Contract without a reason

The Buyer has the right to terminate the Contract at any time without reason or liability by giving the Supplier not less than 90 days' written notice and if it's terminated clause 11.5(b) to 11.5(g) applies.

11.4 When the Buyer can end the Contract

(a) If any of the following events happen, the Buyer has the right to immediately terminate its Contract by issuing a termination notice in writing to the Supplier:

(i) there's a Supplier Insolvency Event;

(ii) if the Supplier repeatedly breaches the Contract in a way to reasonably justify the opinion that its conduct is inconsistent with it having the intention or ability to give effect to the terms and conditions of the Contract;

(iii) if the Supplier is in material breach of any obligation which is capable of remedy, and that breach is not remedied within 30 days of the Supplier receiving notice specifying the breach and requiring it to be remedied;

(iv) there's a change of control (within the meaning of section 450 of the Corporation Tax Act 2010) of the Supplier which isn't pre-approved by the Buyer in writing;

(v) if the Buyer discovers that the Supplier was in one of the situations in 57 (1) or 57(2) of the Regulations at the time the Contract was awarded;

(vi) the Court of Justice of the European Union uses Article 258 of the Treaty on the Functioning of the European Union (TFEU) to declare that the Contract should not have been awarded to the Supplier because of a serious breach of the TFEU or the Regulations;

(vii) the Supplier or its affiliates embarrass or bring the Buyer into disrepute or diminish the public trust in them.

(b) If any of the events in 73(1) (a) to (c) of the Regulations (substantial modification, exclusion of the Supplier, procurement infringement) happen, the Buyer has the right to immediately terminate the Contract and clause 11.5(b) to 11.5(g) applies.

11.5 What happens if the Contract ends

Where the Buyer terminates the Contract under clause 11.4(a) all of the following apply:

(a) the Supplier is responsible for the Buyer's reasonable costs of procuring replacement deliverables for the rest of the term of the Contract;

(b) the Buyer's payment obligations under the terminated Contract stop immediately;

(c) accumulated rights of the Parties are not affected;

(d) the Supplier must promptly delete or return the Government Data except where required to retain copies by law;

(e) the Supplier must promptly return any of the Buyer's property provided under the Contract;

(f) the Supplier must, at no cost to the Buyer, give all reasonable assistance to the Buyer and any incoming supplier and co-operate fully in the handover and re-procurement;

(g) the following clauses survive the termination of the Contract: [3.2.10, 6, 7.2, 9, 11, 14, 15, 16, 17, 18, 34, 35] and any clauses which are expressly or by implication intended to continue.

11.6 When the Supplier can end the Contract

(a) The Supplier can issue a reminder notice if the Buyer does not pay an undisputed invoice on time. The Supplier can terminate the Contract if the Buyer fails to pay an undisputed invoiced sum due and worth over 10% of the total Contract value or £1,000, whichever is the lower, within 30 days of the date of the reminder notice.

(b) If a Supplier terminates the Contract under clause 11.6(a):

  (i) the Buyer must promptly pay all outstanding charges incurred to the Supplier;

  (ii) the Buyer must pay the Supplier reasonable committed and unavoidable losses as long as the Supplier provides a fully itemised and costed schedule with evidence - the maximum value of this payment is limited to the total sum payable to the Supplier if the Contract had not been terminated;

  (iii) clauses 11.5(d) to 11.5(g) apply.

11.7 Partially ending and suspending the Contract

(a) Where the Buyer has the right to terminate the Contract it can terminate or suspend (for any period), all or part of it. If the Buyer suspends the Contract it can provide the Deliverables itself or buy them from a third party.

(b) The Buyer can only partially terminate or suspend the Contract if the remaining parts of it can still be used to effectively deliver the intended purpose.

(c) The Parties must agree (in accordance with clause 24) any necessary variation required by clause 11.7, but the Supplier may not either:

  (i) reject the variation;

  (ii) increase the Charges, except where the right to partial termination is under clause 11.3.

(d) The Buyer can still use other rights available, or subsequently available to it if it acts on its rights under clause 11.7.

12. How much you can be held responsible for

12.1 Each Party's total aggregate liability under or in connection with the Contract (whether in tort, contract or otherwise) is no more than 125% of the Charges paid or payable to the Supplier.

12.2 No Party is liable to the other for:
(a) any indirect losses;
(b) loss of profits, turnover, savings, business opportunities or damage to goodwill (in each case whether direct or indirect).

12.3 In spite of clause 12.1, neither Party limits or excludes any of the following:
(a) its liability for death or personal injury caused by its negligence, or that of its employees, agents or subcontractors;
(b) its liability for bribery or fraud or fraudulent misrepresentation by it or its employees;
(c) any liability that cannot be excluded or limited by law.

12.4 In spite of clause 12.1, the Supplier does not limit or exclude its liability for any indemnity given under clauses 4.2(j), 4.2(m), 8.5, 9.3, 10.5, 13.2, 14.26(e) or 30.2(b).

12.5 Each Party must use all reasonable endeavours to mitigate any loss or damage which it suffers under or in connection with the Contract, including any indemnities.

12.6 If more than one Supplier is party to the Contract, each Supplier Party is fully responsible for both their own liabilities and the liabilities of the other Suppliers.

13. Obeying the law

13.1 The Supplier must, in connection with provision of the Deliverables, use reasonable endeavours to:
(a) comply and procure that its subcontractors comply with the Supplier Code of Conduct appearing at (https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/779660/20190220-Supplier_Code_of_Conduct.pdf) and such other corporate social responsibility requirements as the Buyer may notify to the Supplier from time to time;
(b) support the Buyer in fulfilling its Public Sector Equality duty under S149 of the Equality Act 2010;
(c) not use nor allow its subcontractors to use modern slavery, child labour or inhumane treatment;
(d) meet the applicable Government Buying Standards applicable to Deliverables which can be found online at: https://www.gov.uk/government/collections/sustainable-procurement-the-government-buying-standards-gbs

13.2 The Supplier indemnifies the Buyer against any costs resulting from any default by the Supplier relating to any applicable law to do with the Contract.

13.3 The Supplier must appoint a Compliance Officer who must be responsible for ensuring that the Supplier complies with Law, Clause 13.1 and Clauses 27 to 32

13.4 "Compliance Officer" the person(s) appointed by the Supplier who is responsible for ensuring that the Supplier complies with its legal obligations;

14. Data protection

14.1 The Buyer is the Controller and the Supplier is the Processor for the purposes of the Data Protection Legislation.

14.2 The Supplier must process Personal Data and ensure that Supplier Staff process Personal Data only in accordance with this Contract.

14.3 The Supplier must not remove any ownership or security notices in or relating to the Government Data.

14.4 The Supplier must make accessible back-ups of all Government Data, stored in an agreed off-site location and send the Buyer copies every six Months.

14.5 The Supplier must ensure that any Supplier system holding any Government Data, including back-up data, is a secure system that complies with the security requirements specified [in writing] by the Buyer.

14.6 If at any time the Supplier suspects or has reason to believe that the Government Data provided under the Contract is corrupted, lost or sufficiently degraded, then the Supplier must notify the Buyer and immediately suggest remedial action.

14.7 If the Government Data is corrupted, lost or sufficiently degraded so as to be unusable the Buyer may either or both:

(a) tell the Supplier to restore or get restored Government Data as soon as practical but no later than five Working Days from the date that the Buyer receives notice, or the Supplier finds out about the issue, whichever is earlier;

(b) restore the Government Data itself or using a third party.

14.8 The Supplier must pay each Party's reasonable costs of complying with clause 14.7 unless the Buyer is at fault.

14.9 Only the Buyer can decide what processing of Personal Data a Supplier can do under the Contract and must specify it for the Contract using the template in Annex 1 of the Order Form (*Authorised Processing*).

14.10 The Supplier must only process Personal Data if authorised to do so in the Annex to the Order Form (*Authorised Processing*) by the Buyer. Any further written instructions relating to the processing of Personal Data are incorporated into Annex 1 of the Order Form.

14.11 The Supplier must give all reasonable assistance to the Buyer in the preparation of any Data Protection Impact Assessment before starting any processing, including:

(a) a systematic description of the expected processing and its purpose;

(b) the necessity and proportionality of the processing operations;

(c) the risks to the rights and freedoms of Data Subjects;

(d) the intended measures to address the risks, including safeguards, security measures and mechanisms to protect Personal Data.

14.12 The Supplier must notify the Buyer immediately if it thinks the Buyer's instructions breach the Data Protection Legislation.

14.13 The Supplier must put in place appropriate Protective Measures to protect against a Data Loss Event which must be approved by the Buyer.

14.14 If lawful to notify the Buyer, the Supplier must notify it if the Supplier is required to process Personal Data by Law promptly and before processing it.

14.15 The Supplier must take all reasonable steps to ensure the reliability and integrity of any Supplier Staff who have access to the Personal Data and ensure that they:
(a) are aware of and comply with the Supplier's duties under this clause 11;
(b) are subject to appropriate confidentiality undertakings with the Supplier or any Subprocessor;
(c) are informed of the confidential nature of the Personal Data and do not provide any of the Personal Data to any third Party unless directed in writing to do so by the Buyer or as otherwise allowed by the Contract;
(d) have undergone adequate training in the use, care, protection and handling of Personal Data.

14.16 The Supplier must not transfer Personal Data outside of the EU unless all of the following are true:
(a) it has obtained prior written consent of the Buyer;
(b) the Buyer has decided that there are appropriate safeguards (in accordance with Article 46 of the GDPR);
(c) the Data Subject has enforceable rights and effective legal remedies when transferred;
(d) the Supplier meets its obligations under the Data Protection Legislation by providing an adequate level of protection to any Personal Data that is transferred;
(e) where the Supplier is not bound by Data Protection Legislation it must use its best endeavours to help the Buyer meet its own obligations under Data Protection Legislation; and
(f) the Supplier complies with the Buyer's reasonable prior instructions about the processing of the Personal Data.

14.17 The Supplier must notify the Buyer immediately if it:
(a) receives a Data Subject Access Request (or purported Data Subject Access Request);
(b) receives a request to rectify, block or erase any Personal Data;
(c) receives any other request, complaint or communication relating to either Party's obligations under the Data Protection Legislation;
(d) receives any communication from the Information Commissioner or any other regulatory authority in connection with Personal Data processed under this Contract;
(e) receives a request from any third Party for disclosure of Personal Data where compliance with the request is required or claims to be required by Law;
(f) becomes aware of a Data Loss Event.

14.18 Any requirement to notify under clause 14.17 includes the provision of further information to the Buyer in stages as details become available.

14.19 The Supplier must promptly provide the Buyer with full assistance in relation to any Party's obligations under Data Protection Legislation and any complaint, communication or request made under clause 14.17. This includes giving the Buyer:
(a) full details and copies of the complaint, communication or request;
(b) reasonably requested assistance so that it can comply with a Data Subject Access Request within the relevant timescales in the Data Protection Legislation;
(c) any Personal Data it holds in relation to a Data Subject on request;
(d) assistance that it requests following any Data Loss Event;
(e) assistance that it requests relating to a consultation with, or request from, the Information Commissioner's Office.

14.20 The Supplier must maintain full, accurate records and information to show it complies with this clause 14. This requirement does not apply where the Supplier employs fewer than 250 staff, unless either the Buyer determines that the processing:
(a) is not occasional;
(b) includes special categories of data as referred to in Article 9(1) of the GDPR or Personal Data relating to criminal convictions and offences referred to in Article 10 of the GDPR;
(c) is likely to result in a risk to the rights and freedoms of Data Subjects.

14.21 The Supplier must appoint a Data Protection Officer responsible for observing its obligations in this Schedule and give the Buyer their contact details.

14.22 Before allowing any Subprocessor to process any Personal Data, the Supplier must:
(a) notify the Buyer in writing of the intended Subprocessor and processing;
(b) obtain the written consent of the Buyer;
(c) enter into a written contract with the Subprocessor so that this clause 14 applies to the Subprocessor;
(d) provide the Buyer with any information about the Subprocessor that the Buyer reasonably requires.

14.23 The Supplier remains fully liable for all acts or omissions of any Subprocessor.

14.24 At any time the Buyer can, with 30 Working Days notice to the Supplier, change this clause 14 to:
(a) replace it with any applicable standard clauses (between the controller and processor) or similar terms forming part of an applicable certification scheme under GDPR Article 42;
(b) ensure it complies with guidance issued by the Information Commissioner's Office.

14.25 The Parties agree to take account of any non-mandatory guidance issued by the Information Commissioner's Office.

14.26 The Supplier:
(a) must provide the Buyer with all Government Data in an agreed open format within 10 Working Days of a written request;

(b) must have documented processes to guarantee prompt availability of Government Data if the Supplier stops trading;
(c) must securely destroy all Storage Media that has held Government Data at the end of life of that media using Good Industry Practice;
(d) securely erase all Government Data and any copies it holds when asked to do so by the Buyer unless required by Law to retain it;
(e) indemnifies the Buyer against any and all Losses incurred if the Supplier breaches clause 14 and any Data Protection Legislation.

15. What you must keep confidential

15.1 Each Party must:
(a) keep all Confidential Information it receives confidential and secure;
(b) not disclose, use or exploit the disclosing Party's Confidential Information without the disclosing Party's prior written consent, except for the purposes anticipated under the Contract;
(c) immediately notify the disclosing Party if it suspects unauthorised access, copying, use or disclosure of the Confidential Information.

15.2 In spite of clause 15.1, a Party may disclose Confidential Information which it receives from the disclosing Party in any of the following instances:
(a) where disclosure is required by applicable Law or by a court with the relevant jurisdiction if the recipient Party notifies the disclosing Party of the full circumstances, the affected Confidential Information and extent of the disclosure;
(b) if the recipient Party already had the information without obligation of confidentiality before it was disclosed by the disclosing Party;
(c) if the information was given to it by a third party without obligation of confidentiality;
(d) if the information was in the public domain at the time of the disclosure;
(e) if the information was independently developed without access to the disclosing Party's Confidential Information;
(f) to its auditors or for the purposes of regulatory requirements;
(g) on a confidential basis, to its professional advisers on a need-to-know basis;
(h) to the Serious Fraud Office where the recipient Party has reasonable grounds to believe that the disclosing Party is involved in activity that may be a criminal offence under the Bribery Act 2010.

15.3 The Supplier may disclose Confidential Information on a confidential basis to Supplier Staff on a need-to-know basis to allow the Supplier to meet its obligations under the Contract. The Supplier Staff must enter into a direct confidentiality agreement with the Buyer at its request.

15.4 The Buyer may disclose Confidential Information in any of the following cases:
(a) on a confidential basis to the employees, agents, consultants and contractors of the Buyer;
(b) on a confidential basis to any other Central Government Body, any successor body to a Central Government Body or any company that the Buyer transfers or proposes to transfer all or any part of its business to;
(c) if the Buyer (acting reasonably) considers disclosure necessary or appropriate to carry out its public functions;

(d) where requested by Parliament;
(e) under clauses 5.7 and 16.

15.5 For the purposes of clauses 15.2 to 15.4 references to disclosure on a confidential basis means disclosure under a confidentiality agreement or arrangement including terms as strict as those required in clause 15.

15.6 Information which is exempt from disclosure by clause 16 is not Confidential Information.

15.7 The Supplier must not make any press announcement or publicise the Contract or any part of it in any way, without the prior written consent of the Buyer and must take all reasonable steps to ensure that Supplier Staff do not either.

16. When you can share information

16.1 The Supplier must tell the Buyer within 48 hours if it receives a Request For Information.

16.2 Within the required timescales the Supplier must give the Buyer full co-operation and information needed so the Buyer can:
(a) comply with any Freedom of Information Act (FOIA) request;
(b) comply with any Environmental Information Regulations (EIR) request.

16.3 The Buyer may talk to the Supplier to help it decide whether to publish information under clause 16. However, the extent, content and format of the disclosure is the Buyer's decision, which does not need to be reasonable.

17. Invalid parts of the contract

If any part of the Contract is prohibited by Law or judged by a court to be unlawful, void or unenforceable, it must be read as if it was removed from that Contract as much as required and rendered ineffective as far as possible without affecting the rest of the Contract, whether it's valid or enforceable.

18. No other terms apply

The provisions incorporated into the Contract are the entire agreement between the Parties. The Contract replaces all previous statements and agreements whether written or oral. No other provisions apply.

19. Other people's rights in a contract

No third parties may use the Contracts (Rights of Third Parties) Act (CRTPA) to enforce any term of the Contract unless stated (referring to CRTPA) in the Contract. This does not affect third party rights and remedies that exist independently from CRTPA.

20. Circumstances beyond your control

20.1 Any Party affected by a Force Majeure Event is excused from performing its obligations under the Contract while the inability to perform continues, if it both:

(a) provides written notice to the other Party;
(b) uses all reasonable measures practical to reduce the impact of the Force Majeure Event.

20.2 Either party can partially or fully terminate the Contract if the provision of the Deliverables is materially affected by a Force Majeure Event which lasts for 90 days continuously.

20.3 Where a Party terminates under clause 20.2:
(a) each party must cover its own losses;
(b) clause 11.5(b) to 11.5(g) applies.

21. Relationships created by the contract

The Contract does not create a partnership, joint venture or employment relationship. The Supplier must represent themselves accordingly and ensure others do so.

22. Giving up contract rights

A partial or full waiver or relaxation of the terms of the Contract is only valid if it is stated to be a waiver in writing to the other Party.

23. Transferring responsibilities

23.1 The Supplier cannot assign the Contract without the Buyer's written consent.

23.2 The Buyer can assign, novate or transfer its Contract or any part of it to any Crown Body, public or private sector body which performs the functions of the Buyer.

23.3 When the Buyer uses its rights under clause 23.2 the Supplier must enter into a novation agreement in the form that the Buyer specifies.

23.4 The Supplier can terminate the Contract novated under clause 23.2 to a private sector body that is experiencing an Insolvency Event.

23.5 The Supplier remains responsible for all acts and omissions of the Supplier Staff as if they were its own.

23.6 If the Buyer asks the Supplier for details about Subcontractors, the Supplier must provide details of Subcontractors at all levels of the supply chain including:
(a) their name;
(b) the scope of their appointment;
(c) the duration of their appointment.

24. Changing the contract

24.1 Either Party can request a variation to the Contract which is only effective if agreed in writing and signed by both Parties. The Buyer is not required to accept a variation request made by the Supplier.

25. How to communicate about the contract

25.1 All notices under the Contract must be in writing and are considered effective on the Working Day of delivery as long as they're delivered before 5:00pm on a Working Day. Otherwise the notice is effective on the next Working Day. An email is effective when sent unless an error message is received.

25.2 Notices to the Buyer or Supplier must be sent to their address in the Order Form.

25.3 This clause does not apply to the service of legal proceedings or any documents in any legal action, arbitration or dispute resolution.

26. Preventing fraud, bribery and corruption

26.1 The Supplier shall not:

(a) commit any criminal offence referred to in the Regulations 57(1) and 57(2);

(b) offer, give, or agree to give anything, to any person (whether working for or engaged by the Buyer or any other public body) an inducement or reward for doing, refraining from doing, or for having done or refrained from doing, any act in relation to the obtaining or execution of the Contract or any other public function or for showing or refraining from showing favour or disfavour to any person in relation to the Contract or any other public function.

26.2 The Supplier shall take all reasonable steps (including creating, maintaining and enforcing adequate policies, procedures and records), in accordance with good industry practice, to prevent any matters referred to in clause 26.1 and any fraud by the Staff and the Supplier (including its shareholders, members and directors) in connection with the Contract and shall notify the Buyer immediately if it has reason to suspect that any such matters have occurred or is occurring or is likely to occur.

26.3 If the Supplier or the Staff engages in conduct prohibited by clause 26.1 or commits fraud in relation to the Contract or any other contract with the Crown (including the Buyer) the Buyer may:

(a) terminate the Contract and recover from the Supplier the amount of any loss suffered by the Buyer resulting from the termination, including the cost reasonably incurred by the Buyer of making other arrangements for the supply of the Deliverables and any additional expenditure incurred by the Buyer throughout the remainder of the Contract; or

(b) recover in full from the Supplier any other loss sustained by the Buyer in consequence of any breach of this clause.

27. Equality, diversity and human rights

27.1 The Supplier must follow all applicable equality law when they perform their obligations under the Contract, including:

(a) protections against discrimination on the grounds of race, sex, gender reassignment, religion or belief, disability, sexual orientation, pregnancy, maternity, age or otherwise;

(b) any other requirements and instructions which the Buyer reasonably imposes related to equality Law.

27.2 The Supplier must take all necessary steps, and inform the Buyer of the steps taken, to prevent anything that is considered to be unlawful discrimination by any court or tribunal, or the Equality and Human Rights Commission (or any successor organisation) when working on the Contract.

28. Health and safety

28.1 The Supplier must perform its obligations meeting the requirements of:
(a) all applicable law regarding health and safety;
(b) the Buyer's current health and safety policy while at the Buyer's premises, as provided to the Supplier.

28.2 The Supplier and the Buyer must as soon as possible notify the other of any health and safety incidents or material hazards they're aware of at the Buyer premises that relate to the performance of the Contract.

29. Environment

29.1 When working on Site the Supplier must perform its obligations under the Buyer's current Environmental Policy, which the Buyer must provide.

29.2 The Supplier must ensure that Supplier Staff are aware of the Buyer's Environmental Policy.

30. Tax

30.1 The Supplier must not breach any tax or social security obligations and must enter into a binding agreement to pay any late contributions due, including where applicable, any interest or any fines. The Buyer cannot terminate the Contract where the Supplier has not paid a minor tax or social security contribution.

30.2 Where the Supplier or any Supplier Staff are liable to be taxed or to pay National Insurance contributions in the UK relating to payment received under the Off Contract, the Supplier must both:
(a) comply with the Income Tax (Earnings and Pensions) Act 2003 and all other statutes and regulations relating to income tax, the Social Security Contributions and Benefits Act 1992 (including IR35) and National Insurance contributions;
(b) indemnify the Buyer against any Income Tax, National Insurance and social security contributions and any other liability, deduction, contribution, assessment or claim arising from or made during or after the Contract Period in connection with the provision of the Deliverables by the Supplier or any of the Supplier Staff.

30.3 If any of the Supplier Staff are Workers who receive payment relating to the Deliverables, then the Supplier must ensure that its contract with the Worker contains the following requirements:
(a) the Buyer may, at any time during the term of the Contract, request that the Worker provides information which demonstrates they comply with clause 30.2, or why those requirements do not apply, the Buyer can specify the information the Worker must provide and the deadline for responding;

(b) the Worker's contract may be terminated at the Buyer's request if the Worker fails to provide the information requested by the Buyer within the time specified by the Buyer;
(c) the Worker's contract may be terminated at the Buyer's request if the Worker provides information which the Buyer considers isn't good enough to demonstrate how it complies with clause 30.2 or confirms that the Worker is not complying with those requirements;
(d) the Buyer may supply any information they receive from the Worker to HMRC for revenue collection and management.

31. Conflict of interest

31.1 The Supplier must take action to ensure that neither the Supplier nor the Supplier Staff are placed in the position of an actual or potential conflict between the financial or personal duties of the Supplier or the Supplier Staff and the duties owed to the Buyer under the Contract, in the reasonable opinion of the Buyer.

31.2 The Supplier must promptly notify and provide details to the Buyer if a conflict of interest happens or is expected to happen.

31.3 The Buyer can terminate its Contract immediately by giving notice in writing to the Supplier or take any steps it thinks are necessary where there is or may be an actual or potential conflict of interest.

32. Reporting a breach of the contract

32.1 As soon as it is aware of it the Supplier and Supplier Staff must report to the Buyer any actual or suspected breach of law, clause 13.1, or clauses 26 to 31.

32.2 The Supplier must not retaliate against any of the Supplier Staff who in good faith reports a breach listed in clause 32.1.

33. Resolving disputes

33.1 If there is a dispute between the Parties, their senior representatives who have authority to settle the dispute will, within 28 days of a written request from the other Party, meet in good faith to resolve the dispute.

33.2 If the dispute is not resolved at that meeting, the Parties can attempt to settle it by mediation using the Centre for Effective Dispute Resolution (CEDR) Model Mediation Procedure current at the time of the dispute. If the Parties cannot agree on a mediator, the mediator will be nominated by CEDR. If either Party does not wish to use, or continue to use mediation, or mediation does not resolve the dispute, the dispute must be resolved using clauses 33.3 to 33.5.

33.3 Unless the Buyer refers the dispute to arbitration using clause 33.4, the Parties irrevocably agree that the courts of England and Wales have the exclusive jurisdiction to:
(a) determine the dispute;
(b) grant interim remedies;
(c) grant any other provisional or protective relief.

33.4 The Supplier agrees that the Buyer has the exclusive right to refer any dispute to be finally resolved by arbitration under the London Court of International Arbitration Rules current at the time of the dispute. There will be only one arbitrator. The seat or legal place of the arbitration will be London and the proceedings will be in English.

33.5 The Buyer has the right to refer a dispute to arbitration even if the Supplier has started or has attempted to start court proceedings under clause 33.3, unless the Buyer has agreed to the court proceedings or participated in them. Even if court proceedings have started, the Parties must do everything necessary to ensure that the court proceedings are stayed in favour of any arbitration proceedings if they are started under clause 33.4.

33.6 The Supplier cannot suspend the performance of the Contract during any dispute.

34. Which law applies

This Contract and any issues arising out of, or connected to it, are governed by English law.

APPENDIX A - VARIATION REQUEST FORM

Contract / Project Title: Contract / Project Ref No (FS /FSA No):
Full Description of Variation Request: A full justification and impact assessment including any supplementary evidence must be provided. Any supporting information should be appended to this form.
Area (s) Impacted: - Price ☐ Duration ☐ Price & Duration ☐ Scope of work ☐ Key Personnel ☐ Other ☐
Requester: Signature: Team / Organisation Date:
Supplier Contact Details Supplier Name : Contact Name : Contact Address : : Telephone No : Email Address :
FSA Use Only (Business Area) Amount Approved: Authorised By:- ☐ Cost Centre Manager ☐ Investment Board Signed : Date of Approval: **Please submit this form to** fsa.procurement@food.gov.uk

Procurement Use Only (confirm contract allows for requested variation) Variation Request No: Variation Request Approved by: Date of Approval:
On full approval of this Request for Variation, Procurement will produce a Variation Form for agreement and approval by both parties to append to the Agreement / Contract.

APPENDIX B VARIATION FORM

PROJECT TITLE:

DATE:

VARIATION No:

BETWEEN:

The Food Standards Agency (hereinafter called "the Client") & SUPPLIER (hereinafter called "the Supplier")

1. The Contract is varied as follows:

Contract x

2. Words and expressions in this Variation shall have the meanings given to them in the Framework.

3. The Contract, including any previous Variations, shall remain effective and unaltered except as amended by this Variation.

SIGNED:

For: The Client	For: The Supplier
By:	By: . . . . .
Full Name:	Full Name: . . . . .
Position:	Title: . . . . .
Date:	Date: . . . . .